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(54) Title: QUINOLINONE DERIVATIVES

(57) Abstract: Organic compounds having the formulas I and II are provided where the variables have the values described herein. Pharmaceutical formulations include the organic compounds or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compounds or pharmaceutically acceptable salts of the organic compounds with a carrier and water. A method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient in need thereof.

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QUINOLINONE DERIVATIVES AS TYROSINE KINASE INHIBITORS

FIELD OF THE INVENTION

This invention pertains generally to treating diseases characterized by angiogenesis including cancer. More specifically, the invention described herein pertains to treating diseases characterized by activity of vascular endothelial growth factor receptor tyrosine kinases. The present invention provides, small molecule inhibitors of vascular endothelial growth factor receptor tyrosine kinase, pharmaceutical formulations containing such inhibitors, methods of treating patients with such pharmaceutical formulations, and to methods of preparing such pharmaceutical formulations and inhibitors.

BACKGROUND OF THE INVENTION

Capillaries reach into almost all tissues of the human body and supply tissues with oxygen and nutrients as well as removing waste products. Under 15 typical conditions, the endothelial cells lining the capillaries do not divide, and capillaries, therefore, do not normally increase in number or size in a human adult. Under certain normal conditions, however, such as when a tissue is damaged, or during certain parts of the menstrual cycle, the capillaries begin to proliferate rapidly. This process of forming new capillaries from pre-existing blood vessels is 20 known as angiogenesis or neovascularization. See Folkman, J. Scientific American 275, 150-154 (1996). Angiogenesis during wound healing is an example of pathophysiological neovascularization during adult life. During wound healing, the additional capillaries provide a supply of oxygen and nutrients, promote granulation tissue, and aid in waste removal. After termination of the healing process, the 25 capillaries normally regress. Lymboussaki, A. "Vascular Endothelial Growth Factors and their Receptors in Embryos, Adults, and in Tumors" Academic

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Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999).

Angiogenesis also plays an important role in the growth of cancer cells. It is known that once a nest of cancer cells reaches a certain size, roughly 1 to 2 mm in diameter, the cancer cells must develop a blood supply in order for the tumor to grow larger as diffusion will not be sufficient to supply the cancer cells with enough oxygen and nutrients. Thus, inhibition of angiogenesis is expected to halt the growth of cancer cells.

Receptor tyrosine kinases (RTKs) are transmembrane polypeptides 10 that regulate developmental cell growth and differentiation, remodeling and regeneration of adult tissues. Mustonen, T. et al., J. Cell Biology 129, 895-898 (1995); van der Geer, P. et al. Ann Rev. Cell Biol. 10, 251-337 (1994). Polypeptide ligands known as growth factors or cytokines, are known to activate RTKs. Signaling RTKs involves ligand binding and a shift in conformation in the 15 external domain of the receptor resulting in its dimerization. Lymboussaki, A. "Vascular Endothelial Growth Factors and their Receptors in Embryos, Adults, and in Tumors" Academic Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999); Ullrich, A. et al., Cell 61, 203-212 (1990). Binding of the ligand to the RTK 20 results in receptor trans-phosphorylation at specific tyrosine residues and subsequent activation of the catalytic domains for the phosphorylation of cytoplasmic substrates. Id.

Two subfamilies of RTKs are specific to the vascular endothelium. These include the vascular endothelial growth factor (VEGF) subfamily and the Tie receptor subfamily. Class III RTKs include VEGFR-1, VEGFR-2, and VEGFR-3. Shibuya, M. et al., Oncogene 5, 519-525 (1990); Terman, B. et al., Oncogene 6, 1677-1683 (1991); Aprelikova, O. et al., Cancer Res. 52, 746-748 (1992).

Members of the VEGF subfamily have been described as being able to induce vascular permeability and endothelial cell proliferation and further

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identified as a major inducer of angiogenesis and vasculogenesis. Ferrara, N. et al., Endocrinol. Rev. 18, 4-25 (1997). VEGF is known to specifically bind to RTKs including VEGFR-1 and VEGFR-2. DeVries, C. et al., Science 255, 989-991 (1992); Quinn, T. et al., Proc. Natl. Acad. Sci. 90, 7533-7537 (1993). VEGF stimulates the migration and proliferation of endothelial cells and induces angiogenesis both *in vitro* and *in vivo*. Connolly, D. et al., J. Biol. Chem. 264, 20017-20024 (1989); Connolly, D. et al., J. Clin. Invest. 84, 1470-1478 (1989); Ferrara, N. et al., Endocrino. Rew. 18, 4-25 (1997); Leung, D. et al., Science 246, 1306-1309 (1989); Plouet, J. et al., EMBO J 8, 3801-3806 (1989).

Because angiogenesis is known to be critical to the growth of cancer and to be controlled by VEGF and VEGF-RTK, substantial efforts have been undertaken to develop therapeutics that are antagonists of VEGF-RTK to thereby inhibit or retard angiogenesis, and, hopefully, interfere or stop tumor proliferation.

reported as having activity against one of more the VEGF-RTKs. Examples include quinoline derivatives such as described in WO 98/13350, aminonicotinamide derivatives (see, e.g., WO 01/55114), antisense compounds (see, e.g., WO 01/52904), peptidomimetics (see, e.g., WO 01/52875), quinazoline derivatives (see, e.g., U.S. Patent No. 6,258,951) monoclonal antibodies (see, e.g., EP 1 086 705 A1), various 5,10,15,20-tetraaryl-porphyrins and 5,10,15-triaryl-corroles (see, e.g., WO 00/27379), heterocyclic alkanesulfonic and alkane carboxylic acid derivatives (see, e.g., DE19841985), oxindolylquinazoline derivatives (see, e.g., WO 99/10349), 1,4-diazaanthracine derivatives (see, e.g., U.S. Patent No. 5,763,441), and cinnoline derivatives (see, e.g., WO 97/34876), and various indazole compounds (see, e.g., WO 01/02369 and WO 01/53268).

Various indolyl substituted compounds have recently been disclosed in WO 01/29025, WO 01/62251, and WO 01/62252, and various benzimidazolyl compounds have recently been disclosed in WO 01/28993. These compounds are reportedly capable of inhibiting, modulating, and/or regulating signal transduction

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of both receptor-type and non-receptor tyrosine kinases. Some of the disclosed compounds contain a quinolone fragment bonded to the indolyl or benzimidazolyl group.

The synthesis of 4-hydroxy quinolone and 4-hydroxy quinoline

derivatives is disclosed in a number of references. For example, Ukrainets et al. have disclosed the synthesis of 3-(benzimidazol-2-yl)-4-hydroxy-2-oxo-1,2-dihydroquinoline. Ukrainets, I. et al., Tet. Lett. 42, 7747-7748 (1995); Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 2, 239-241(1992). Ukrainets has also disclosed the synthesis, anticonvulsive and antithyroid activity of other 4-hydroxy quinolones and thio analogs such as 1H-2-oxo-3-(2-benzimidazolyl)-4-hyrdoxyquinoline. Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 1, 105-108 (1993); Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 8, 1105-1108 (1993); Ukrainets, I. et al., Chem. Heterocyclic Comp. 33, 600-604, (1997).

The synthesis of various quinoline derivatives is disclosed in WO 97/48694. These compounds are disclosed as capable of binding to nuclear hormone receptors and being useful for stimulating osteoblast proliferation and bone growth. The compounds are also disclosed as being useful in the treatment or prevention of diseases associated with nuclear hormone receptor families.

Various quinoline derivatives in which the benzene ring of the quinolone is substituted with a sulfur group are disclosed in WO 92/18483. These compounds are disclosed as being useful in pharmaceutical formulations and as medicaments.

Quinolone and coumarin derivatives have been disclosed as having
use in a variety of applications unrelated to medicine and pharmaceutical
formulations. References that describe the preparation of quinolone derivatives for
use in photopolymerizable compositions or for luminescent properties include: U.S.
Patent No. 5,801,212 issued to Okamoto et al.; JP 8-29973; JP 7-43896; JP 6-9952;
JP 63-258903; EP 797376; and DE 23 63 459.

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Despite the exploration of a variety of chemistries to provide VEGF-RTK-antagonist therapies, a continuing need exists for compounds that inhibit the proliferation of capillaries, inhibit the growth of tumors, and/or inhibit vascular endothelial growth factor receptor tyrosine kinase and pharmaceutical formulations that contain such compounds. A need also exists for methods for administering such compounds and pharmaceutical formulations to patients in need thereof.

SUMMARY OF THE INVENTION

The present invention provides compounds, pharmaceutical formulations including the compounds, methods of preparing the pharmaceutical formulations, and methods of treating patients with the pharmaceutical formulations and compounds.

The present invention provides a first group of compounds having the structure I. The invention also provides tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers. Structure I has the following formula:

$$R^{5}$$
 R^{6}
 R^{7}
 R^{8}
 R^{9}

I

where, in the first group of compounds:

Y is selected from -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted

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heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted saturated heterocyclylaminoalkyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, substituted or unsubstituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

10 R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups, -NR¹⁶R¹⁷ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or 15 unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, 20 substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, or -C(=0)R¹⁸ groups;

R⁵, R⁶, R⁷, and R⁸ may be the same or different and are independently selected from H, Cl, Br, F, I, -NO₂, -OH, -OR¹⁹ groups, -NR²⁰R²¹ groups, -SH, -SR²² groups, -S(=O)R²³ groups, -S(=O)₂R²⁴ groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted

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or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted (heterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R⁹ and R¹⁴ may be the same or different and are independently

15 selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or
unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups,
substituted or unsubstituted arylamino groups, substituted or unsubstituted
dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or
unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups,

20 substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or
-C(=O)-aryl groups;

R¹⁰ is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(alkyl)(aryl) groups, -N(aryl)₂ groups, -NH(heterocyclyl) groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl)₂ groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(heterocyclyl)₃ groups, -C(=O)N(heterocyclyl)₄ groups, -C(=O)N(heterocyclyl)₅ groups, -C(=O)N(heterocycl

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-C(=O)N(aryl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

R¹¹ is selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups,
-N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)

5 groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups,
-N(aryl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, heterocyclyloxyalkyl groups, or substituted or unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from substituted or unsubstituted alkyl groups. substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH₂, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted 15 or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted 20 dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH2, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl 25 groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)₂ groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or

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unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, or -C(=O)-N(alkyl)(heterocyclyl) groups;

R¹⁵ and R¹⁹ may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted 5 aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)2 groups, 10 -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or 15 unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted 20 aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹⁷ and R²¹ may be the same or different and are independently

25 selected from H, substituted or unsubstituted alkyl groups, substituted or
unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups,

-C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups,-C(=O)NH₂,

-C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups,

-C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups,

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-C(=0)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted 5 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=0)-heterocyclyl groups, -C(=0)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, $-C(=O)-N(heterocyclyl)_2$ groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted 10 diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, or 15 -C(=O)-N(alkyl)(heterocyclyl) groups;

R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, -N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted or unsubstituted or unsubstituted aryloxy groups, heterocyclyloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-aryl groups, or -N(aryl)O-aryl groups; and

R²² is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

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The invention provides a second group of compounds including compounds having the structure I, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers.

5 . In the second group of compounds:

Y is selected from -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, substituted or unsubstituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups, -NR¹⁶R¹⁷ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted or unsubstituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted or unsubstituted

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R⁵, R⁶, R⁷, and R⁸ may be the same or different and are independently selected from H, Cl, Br, F, I, -NO₂, -OH, -OR¹⁹ groups, -NR²⁰R²¹ groups, -SH, -SR²² groups, -S(=O)R²³ groups, -S(=O)₂R²⁴ groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, $-C(=O)R^{25}$ groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R⁹ is selected from the group consisting of -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁰ is selected from substituted or unsubstituted aryl groups,

25 substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups,

-C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂,

-C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups,

-C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, -NH₂, -NH(alkyl) groups,

-NH(aryl) groups, -N(alkyl)₂ groups, -N(alkyl)(aryl) groups, -N(aryl)₂ groups,

30 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)₂ groups,

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-C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

R¹¹ is selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, substituted or unsubstituted alkyl groups, or substituted or unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH2, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, 15 substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=0)N(aryl)₂ groups, -C(=0)N(alkyl)(aryl) groups, substituted or 20 unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, 25 $-C(=O)-N(heterocyclyl)_2$ groups, -C(=O)N(aryl)(heterocyclyl) groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups,

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substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁴ is selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁵ and R¹⁹ may be the same or different and are independently 10 selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) 15 groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl 20 groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted 25 aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

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R¹⁷ and R²¹ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, 5 -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, 10 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups. -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)₂ groups, -C(=O)N(aryl)(heterocyclyl) groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or 15 unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are

independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups,
-N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)
groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,
-N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or
unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups,
substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryloxy
groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-aryl groups;
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R²² is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

The invention provides a third group of compounds including compounds having the structure I, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers.

In the third group of compounds:

Y is selected from -OH, SH, alkylthio groups, arylthio groups, -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, -CN, substituted or unsubstituted 10 alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, 15 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, substituted or 20 unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups,

-NR¹⁶R¹⁷ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkynyl groups,

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substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, or -C(=O)R¹⁸ groups;

R⁵, R⁶, R⁷, and R⁸ may be the same or different and are independently selected from H, Cl, Br, F, I, -NO2, -OH, -OR19 groups, -NR20R21 groups, -SH, -SR²² groups, -S(=O)R²³ groups, -S(=O)₂R²⁴ groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R²⁵ groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R⁹ and R¹⁴ may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted or unsubstituted dialkylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted alkyl groups, substituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups:

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R¹⁰ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(alkyl)2 groups, -C(=O)N(alkyl)2 groups, -N(alkyl)2 groups, -N(alkyl)3 groups, -N(alkyl)3 groups, -N(alkyl)4 groups, -N(alkyl)5 groups, -N(alkyl)6 groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)6 groups, or -C(=O)N(aryl)6 groups;

R¹¹ is selected from H, -OH, alkoxy groups, aryloxy groups, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, or substituted or unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from H, substituted or unsubstituted alkyl groups,
substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl
groups, -OH, alkoxy groups, aryloxy groups, -NH₂, substituted or unsubstituted
heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted
or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted
dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups,
substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted
(alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups,
substituted or unsubstituted arylamino groups, substituted or unsubstituted
dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or
unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups,

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-C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

10 R¹⁵ and R¹⁹ may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH2, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) 15 groups, $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups, $-C(=O)N(alkyl)(aryl)_2$ groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups. substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl 20 groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted 25 aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

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R¹⁷ and R²¹ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups,-C(=O)NH2, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=0)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups. substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups. 10 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl) groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups, 15 substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are

20 independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups,
-N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)
groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,
-N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or
unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups,

25 substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl
groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl
groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, or -N(aryl)O-aryl groups;
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R²² is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

In the third group of compounds, at least one of R⁵, R⁶, R⁷, or R⁸ is selected from substituted or unsubstituted amidinyl groups, substituted or 5 unsubstituted guanidinyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or 10 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups. or substituted or unsubstituted heterocyclyloxyalkyl groups; -OR19 groups where R19 is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted 15 heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, 20 substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or 25 unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted and unsubstituted heterocyclyloxyalkyl groups; -NR²⁰R²¹ groups where R²⁰ is selected from substituted or unsubstituted heterocyclyl groups; -NR²⁰R²¹ groups where R²¹ is selected from substituted or unsubstituted 30 heterocyclyl groups, -C(=0)H, -C(=0)-aryl groups,-C(=0)NH₂,

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-C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=0)O-aryl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups; or -C(=0)R²⁵ groups where R²⁵ is selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, -N(heterocyclyl)₂ groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aryloxy groups, or substituted or unsubstituted heterocyclyl groups.

The invention provides a fourth group of compounds having the structure I, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers.

In the fourth group of compounds:

Y is selected from -OH, SH, alkylthio groups, arylthio groups, -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, -CN, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted aralkyl groups, substituted alkylaminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted or unsubst

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unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups, -NR¹⁶R¹⁷ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted or unsubstituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted or unsubstituted

R⁵, R⁶, R⁷, and R⁸ may be the same or different and are independently selected from H, Cl, Br, F, I, -NO₂, -OH, -OR¹⁹ groups, -NR²⁰R²¹ groups, -SH, -SR²² groups, -S(=O)R²³ groups, -S(=O)2R²⁴ groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted or unsubstituted dialkylaminoalkyl groups, substituted arylaminoalkyl groups, substituted or unsubstituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R²⁵ groups, substituted or unsubstituted aminoalkyl groups,

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substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R⁹ and R¹⁴ may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NHz, substituted or unsubstituted alkylamino groups, substituted or unsubstituted or unsubstituted dialkylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted alkyl groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁰ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH(aryl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -N(alkyl) groups, -N(alkyl) groups, -N(alkyl)(aryl) groups, -N(aryl)2 groups, -N(aryl)2 groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

R¹¹ is selected from H, -OH, alkoxy groups, aryloxy groups, -NH₂,
-NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups,
-N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl)
groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, or substituted or
unsubstituted aryl groups;

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R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from H, substituted or unsubstituted alkyl groups, 5 substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH2, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, 10 substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, 15 -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)(heterocyclyl) groups, 20 -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁵ and R¹⁹ may be the same or different and are independently

25 selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups,

-C(=O)-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(alkyl)₂ groups, substituted or unsubstituted or unsubstituted

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alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹⁷ and R²¹ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or 15 unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, 20 substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, 25 -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)₂ groups, -C(=O)-N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted 30 heterocyclyloxyalkyl groups:

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R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, -N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted or unsubstituted heterocyclyl groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(aryl)O-alkyl groups; and

 $m R^{22}$ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

In the fourth group of compounds, at least one of R¹, R², R³, or R⁴ is an -OR¹⁵ group and R¹⁵ is selected from substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

Preferred compounds in any of the first, second, or third groups described above are provided in which Z is an -NR¹⁴. Preferred compound of the fourth group are also provided in which Z is an -NR¹⁰ group.

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Preferred compounds according to the first, second, third, and fourth groups of compounds are provided in which Y is an -OR¹⁰ group, an-NR¹²R¹³ group, or a substituted or unsubstituted alkynyl group.

Other preferred compounds of the first, second, third, and fourth groups are provided in which R¹ is selected from H, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted or unsubstituted heterocyclylalkoxy groups.

Still further provided are compounds of the first, second, third, and fourth groups in which R² is selected from the group consisting of H, F, Cl, -NO₂, substituted and unsubstituted heterocyclylalkoxy groups, and substituted and unsubstituted heterocyclyl groups.

Still further provided are compounds of the first, second, third, and fourth groups in which R^6 or R^7 is an alkyl group. Still further preferred compounds of the four groups are those in which R^6 or R^7 is an $\bot OR^{19}$ group and R^{19} is an alkyl group, an aryl group, a heterocyclyl group, or a heterocyclylalkyl group.

Preferred compounds of the fourth group of compounds are provided in which R¹ is an -OR¹5 group and R¹5 is selected from substituted or unsubstituted 20 heterocyclylalkyl groups, substituted or unsubstituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

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The invention further provides compounds having the structure II. The invention provides tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers. Structure II has the following formula

$$\begin{array}{c|c}
R^{5} & X^{1} = X^{2} \\
R^{3} & X^{1} = X^{2} \\
R^{3} & R^{5}
\end{array}$$

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 \mathbf{II}

where:

Y is selected from H, -OH, -OR¹⁰ groups, -SH, -SR¹¹ groups, -NR¹²R¹³ groups, -CN, -C(=O)-R¹⁴ groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

 X^1 , X^2 , X^3 , and X^4 are selected from C or N, and at least one of X^1 , X^2 , X^3 , and X^4 is N;

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R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ may be the same or different and are independently selected from H, Cl, Br, F, I, -NO₂, -CN, -OH, -OR¹⁵ groups. $-NR^{16}R^{17}$ groups, $-C(=O)R^{18}$ groups, -SH, $-SR^{19}$ groups, $-S(=O)R^{20}$ groups, S(=O)₂R²¹ groups, substituted or unsubstituted amidinyl groups, substituted or 5 unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, 10 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, 15 substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups; R⁵ is absent or is H if X1 is N; R6 is absent or is H if X2 is N; R7 is absent or is H if X3 is N; and R⁸ is absent or is H if X⁴ is N;

R⁹ is selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁰ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH₂, -C(=O)NH₃ groups, -C(=O)NH₄ groups, -C(=O)NH₄ groups, -C(=O)NH₄ groups, -C(=O)NH₄ groups,

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-C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -NH2, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(alkyl)(aryl) groups, -N(aryl)2 groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

R¹¹ and R¹⁹ may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, or substituted or unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups,

substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH2, substituted or unsubstituted 15 heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups. substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, 20 substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=0)H, -C(=0)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, $-C(=O)N(alkyl)_2$ groups. 25 $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups.

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substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁴ is selected from H, -OH, alkoxy groups, aryloxy groups, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, or -N(aryl)(heterocyclyl) groups;

R¹² and R¹³ may join together to form a 5 to 7 membered saturated or unsaturated, substituted or unsubstituted N-containing ring;

10 R¹⁵ is selected from substituted or unsubstituted alkyl groups. substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl)groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 15 groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted 20 heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or 25 unsubstituted hydroxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

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R¹⁷ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted 10 (aryl)(alkyl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=0)-heterocyclyl groups, -C(=0)-O-heterocyclyl groups. -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)₂ groups. -C(=O)-N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, 15 substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, or -NH2 groups;

R¹⁶ and R¹⁷ may join together to form a 5 to 7 membered saturated or unsaturated, substituted or unsubstituted N-containing ring; and

R¹⁸, R²⁰, and R²¹ may be the same or different and are independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, or -N(aryl)O-aryl groups.

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Preferred compounds having structure II are also provided where Y is selected from H, -OH, -OR¹⁰ groups, or -NR¹²R¹³ groups.

Still other preferred compounds having structure II are provided where at least two of X¹, X², X³, and X⁴ are C and the corresponding substituents R⁵, R⁶, R⁷, and R⁸ are hydrogen, and at least one of X¹, X², X³, and X⁴ is N, and the rest of the compound is consistent with any of the above-described compounds.

Still other more preferred compounds of structure II are provided in which R^6 or R^7 is an alkyl group and the rest of the compound is consistent with any of the above-described compounds.

Still other compounds of structure II are provided in which R⁶ or R⁷ is an -OR¹⁵ group and R¹⁵ is an alkyl, aryl, heterocyclyl, or heterocyclylalkyl group and the rest of the molecule is consistent with any of the above-described compounds.

Still further compounds having the formula of structure II are provided in which R¹ is selected from H, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, or substituted or unsubstituted heterocyclyl groups.

Still other compounds having the Structure II are provided in which In other compounds having the structure II, R² is selected from H, F, Cl, -NO₂, substituted or unsubstituted heterocyclyl groups, or substituted or unsubstituted heterocyclylalkoxy groups.

Pharmaceutical formulations according to the present invention are provided which include any of the compounds described above in combination with a pharmaceutically acceptable carrier.

A method of treating a patient in need of an inhibitor of vascular endothelial growth factor receptor tyrosine kinase is provided which includes

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administering an effective amount of the pharmaceutical formulation according to the present invention to a patient in need thereof.

Further objects, features and advantages of the invention will be apparent from the following detailed description.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides novel compounds that act as antagonists of receptor tyrosine kinases, and, more particularly, as inhibitors of bFGF and/or VEGF-RTK function. The compounds provided herein can be formulated into pharmaceutical formulations that are useful in treating patients with a need for an inhibitor of VEGF-RTK, especially, in particular embodiments, to provide compositions and methods for reducing capillary proliferation and in the treatment of cancer.

The following abbreviations and definitions are used throughout this application:

"VEGF" is an abbreviation that stands for vascular endothelial growth factor.

"RTK" is an abbreviation that stands for receptor tyrosine kinase.

"VEGF-RTK" is an abbreviation that stands for vascular endothelial growth factor receptor tyrosine kinase.

20 "Flt-1" is an abbreviation that stands for fms-like tyrosine kinase-1, also known as vascular endothelial growth factor receptor-1 or "VEGFR1".

"KDR" is an abbreviation that stands for kinase- insert domaincontaining receptor, also known as vascular endothelial growth factor receptor-2 or "VEGFR2". WO 02/22598 PCT/US01/42131

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"bFGF" is an abbreviation that stands for basic fibroblast growth factor.

"bFGFR" is an abbreviation that stands for basic fibroblast growth factor receptor.

Generally, reference to a certain element such as hydrogen or H is meant to include all isotopes of that element. For example, if an R group is defined to include hydrogen or H, it also includes deuterium and tritium.

The phrase "unsubstituted alkyl" refers to alkyl groups that do not contain heteroatoms. Thus the phrase includes straight chain alkyl groups such as 10 methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl and the like. The phrase also includes branched chain isomers of straight chain alkyl groups, including but not limited to, the following which are provided by way of example: -CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -CH(CH₂CH₃)₂, -C(CH₃)₃, -C(CH₂CH₃)₃, -CH₂CH(CH₃)₂, -CH₂CH(CH₃)(CH₂CH₃), -CH₂CH(CH₂CH₃)₂, 15 -CH₂C(CH₃)₃, -CH₂C(CH₂CH₃)₃, -CH(CH₃)CH(CH₃)(CH₂CH₃), -CH2CH2CH(CH3)2, -CH2CH2CH(CH3)(CH2CH3), -CH2CH2CH(CH2CH3)2, -CH2CH2C(CH3)3, -CH2CH2C(CH2CH3)3, -CH(CH3)CH2CH(CH3)2, -CH(CH₃)CH(CH₃)CH(CH₃)₂, -CH(CH₂CH₃)CH(CH₃)(CH₂CH₃), and others. The phrase also includes cyclic alkyl groups such as cyclopropyl, 20 cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl and such rings substituted with straight and branched chain alkyl groups as defined above. The phrase also includes polycyclic alkyl groups such as, but not limited to, adamantyl norbornyl, and bicyclo[2.2.2]octyl and such rings substituted with straight and branched chain alkyl groups as defined above. Thus, the phrase unsubstituted alkyl 25 groups includes primary alkyl groups, secondary alkyl groups, and tertiary alkyl groups. Unsubstituted alkyl groups may be bonded to one or more carbon atom(s), oxygen atom(s), nitrogen atom(s), and/or sulfur atom(s) in the parent compound. Preferred unsubstituted alkyl groups include straight and branched chain alkyl groups and cyclic alkyl groups having 1 to 20 carbon atoms. More preferred such

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unsubstituted alkyl groups have from 1 to 10 carbon atoms while even more preferred such groups have from 1 to 5 carbon atoms. Most preferred unsubstituted alkyl groups include straight and branched chain alkyl groups having from 1 to 3 carbon atoms and include methyl, ethyl, propyl, and -CH(CH₃)₂.

5 The phrase "substituted alkyl" refers to an unsubstituted alkyl group as defined above in which one or more bonds to a carbon(s) or hydrogen(s) are replaced by a bond to non-hydrogen and non-carbon atoms such as, but not limited to, a halogen atom in halides such as F, Cl, Br, and I; and oxygen atom in groups such as hydroxyl groups, alkoxy groups, aryloxy groups, and ester groups; a sulfur atom in groups such as thiol groups, alkyl and aryl sulfide groups, sulfone groups, 10 sulfonyl groups, and sulfoxide groups; a nitrogen atom in groups such as amines, amides, alkylamines, dialkylamines, arylamines, alkylarylamines, diarylamines, Noxides, imides, and enamines; a silicon atom in groups such as in trialkylsilyl groups, dialkylarylsilyl groups, alkyldiarylsilyl groups, and triarylsilyl groups; and 15 other heteroatoms in various other groups. Substituted alkyl groups also include groups in which one or more bonds to a carbon(s) or hydrogen(s) atom is replaced by a bond to a heteroatom such as oxygen in carbonyl, carboxyl, and ester groups; nitrogen in groups such as imines, oximes, hydrazones, and nitriles. Preferred substituted alkyl groups include, among others, alkyl groups in which one or more 20 bonds to a carbon or hydrogen atom is/are replaced by one or more bonds to fluorine atoms. One example of a substituted alkyl group is the trifluoromethyl group and other alkyl groups that contain the trifluoromethyl group. Other alkyl groups include those in which one or more bonds to a carbon or hydrogen atom is replaced by a bond to an oxygen atom such that the substituted alkyl group contains a hydroxyl, alkoxy, aryloxy group, or heterocyclyloxy group. Still other alkyl groups include alkyl groups that have an amine, alkylamine, dialkylamine, arylamine, (alkyl)(aryl)amine, diarylamine, heterocyclylamine, (alkyl)(heterocyclyl)amine, (aryl)(heterocyclyl)amine, or diheterocyclylamine group.

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The phrase "unsubstituted aryl" refers to aryl groups that do not contain heteroatoms. Thus the phrase includes, but is not limited to, groups such as phenyl, biphenyl, anthracenyl, naphthenyl by way of example. Although the phrase "unsubstituted aryl" includes groups containing condensed rings such as naphthalene, it does not include aryl groups that have other groups such as alkyl or halo groups bonded to one of the ring members, as aryl groups such as tolyl are considered herein to be substituted aryl groups as described below. A preferred unsubstituted aryl group is phenyl. Unsubstituted aryl groups may be bonded to one or more carbon atom(s), oxygen atom(s), nitrogen atom(s), and/or sulfur atom(s) in the parent compound, however.

The phrase "substituted aryl group" has the same meaning with respect to unsubstituted aryl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. However, a substituted aryl group also includes aryl groups in which one of the aromatic carbons is bonded to one of the non-carbon or non-hydrogen atoms described above and also includes aryl groups in which one or more aromatic carbons of the aryl group is bonded to a substituted and/or unsubstituted alkyl, alkenyl, or alkynyl group as defined herein. This includes bonding arrangements in which two carbon atoms of an aryl group are bonded to two atoms of an alkyl, alkenyl, or alkynyl group to define a fused ring system (e.g. dihydronaphthyl or tetrahydronaphthyl). Thus, the phrase "substituted aryl" includes, but is not limited to tolyl, and hydroxyphenyl among others.

The phrase "unsubstituted alkenyl" refers to straight and branched chain and cyclic groups such as those described with respect to unsubstituted alkyl groups as defined above, except that at least one double bond exists between two carbon atoms. Examples include, but are not limited to vinyl, -CH=C(H)(CH₃), -CH=C(CH₃)₂, -C(CH₃)=C(H)₂, -C(CH₃)=C(H)(CH₃), -C(CH₂CH₃)=CH₂, cyclohexenyl, cyclohexadienyl, butadienyl, pentadienyl, and hexadienyl among others.

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The phrase "substituted alkenyl" has the same meaning with respect to unsubstituted alkenyl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. A substituted alkenyl group includes alkenyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon double bonded to another carbon and those in which one of the non-carbon or non-hydrogen atoms is bonded to a carbon not involved in a double bond to another carbon.

The phrase "unsubstituted alkynyl" refers to straight and branched chain groups such as those described with respect to unsubstituted alkyl groups as defined above, except that at least one triple bond exists between two carbon atoms. Examples include, but are not limited to $-C \equiv C(H_1)$, $-C \equiv C(CH_2)$, $-C \equiv C(CH_2)$, $-C(H_2) \equiv C(H_1)$, $-C(H_2) \equiv C(H_2)$, and $-C(H_2) \equiv C(CH_2)$ among others.

The phrase "substituted alkynyl" has the same meaning with respect to unsubstituted alkynyl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. A substituted alkynyl group includes alkynyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon triple bonded to another carbon and those in which a non-carbon or non-hydrogen atom is bonded to a carbon not involved in a triple bond to another carbon.

The phrase "unsubstituted aralkyl" refers to unsubstituted alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to an aryl group as defined above. For example, methyl (-CH₃) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a phenyl group, such as if the carbon of the methyl were bonded to a carbon of benzene, then the compound is an unsubstituted aralkyl group (*i.e.*, a benzyl group). Thus the phrase includes, but is not limited to, groups such as benzyl, diphenylmethyl, and 1-phenylethyl (-CH(C₆H₅)(CH₃)) among others.

The phrase "substituted aralkyl" has the same meaning with respect to unsubstituted aralkyl groups that substituted aryl groups had with respect to unsubstituted aryl groups. However, a substituted aralkyl group also includes

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groups in which a carbon or hydrogen bond of the alkyl part of the group is replaced by a bond to a non-carbon or a non-hydrogen atom. Examples of substituted aralkyl groups include, but are not limited to, -CH₂C(=O)(C₆H₅), and -CH₂(2-methylphenyl) among others.

5 The phrase "unsubstituted heterocyclyl" refers to both aromatic and nonaromatic ring compounds including monocyclic, bicyclic, and polycyclic ring compounds such as, but not limited to, quinuclidyl, containing 3 or more ring members of which one or more is a heteroatom such as, but not limited to, N, O, and S. Although the phrase "unsubstituted heterocyclyl" includes condensed 10 heterocyclic rings such as benzimidazolyl, it does not include heterocyclyl groups that have other groups such as alkyl or halo groups bonded to one of the ring members as compounds such as 2-methylbenzimidazolyl are substituted heterocyclyl groups. Examples of heterocyclyl groups include, but are not limited to: unsaturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not 15 limited to pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g. 4H-1,2,4-triazolyl, 1H-1,2,3triazolyl, 2H-1,2,3-triazolyl etc.), tetrazolyl, (e.g. 1H-tetrazolyl, 2H tetrazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl; condensed 20 unsaturated heterocyclic groups containing 1 to 4 nitrogen atoms such as, but not limited to, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl; unsaturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, oxazolyl, isoxazolyl, oxadiazolyl (e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5oxadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms 25 and 1 to 3 nitrogen atoms such as, but not limited to, morpholinyl; unsaturated condensed heterocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, benzoxazolyl, benzoxadiazolyl, benzoxazinyl (e.g. 2H-1,4benzoxazinyl etc.); unsaturated 3 to 8 membered rings containing 1 to 3 sulfur 30 atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolyl, isothiazolyl, thiadiazolyl (e.g. 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-

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thiadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolodinyl; saturated and unsaturated 3 to 8 membered rings containing 1 to 2 sulfur atoms such as, but not limited to, thienyl, dihydrodithiinyl, dihydrodithionyl, tetrahydrothiophene, tetrahydrothiopyran; unsaturated condensed heterocyclic rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, benzothiazolyl, benzothiadiazolyl, benzothiazinyl (e.g. 2H-1,4-benzothiazinyl, etc.), dihydrobenzothiazinyl (e.g. 2H-3,4-dihydrobenzothiazinyl, etc.), unsaturated 3 to 8 membered rings containing oxygen atoms such as, but not limited to furyl; unsaturated condensed heterocyclic rings containing 1 to 2 oxygen atoms such as 10 benzodioxolyl (e.g. 1,3-benzodioxoyl, etc.); unsaturated 3 to 8 membered rings containing an oxygen atom and 1 to 2 sulfur atoms such as, but not limited to, dihydrooxathiinyl; saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 2 sulfur atoms such as 1,4-oxathiane; unsaturated condensed rings 15 containing 1 to 2 sulfur atoms such as benzothienyl, benzodithiinyl; and unsaturated condensed heterocyclic rings containing an oxygen atom and 1 to 2 oxygen atoms such as benzoxathiinyl. Heterocyclyl group also include those described above in which one or more S atoms in the ring is double-bonded to one or two oxygen atoms (sulfoxides and sulfones). For example, heterocyclyl groups include 20 tetrahydrothiophene, tetrahydrothiophene oxide, and tetrahydrothiophene 1,1dioxide. Preferred heterocyclyl groups contain 5 or 6 ring members. More preferred heterocyclyl groups include morpholine, piperazine, piperidine, pyrrolidine, imidazole, pyrazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, thiomorpholine, thiomorpholine in which the S atom of the thiomorpholine is 25 bonded to one or more O atoms, pyrrole, homopiperazine, oxazolidin-2-one, pyrrolidin-2-one, oxazole, quinuclidine, thiazole, isoxazole, furan, and tetrahydrofuran.

The phrase "substituted heterocyclyl" refers to an unsubstituted heterocyclyl group as defined above in which one of the ring members is bonded to a non-hydrogen atom such as described above with respect to substituted alkyl groups and substituted aryl groups. Examples, include, but are not limited to, 2-

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methylbenzimidazolyl, 5-methylbenzimidazolyl, 5-chlorobenzthiazolyl, 1-methyl piperazinyl, and 2-chloropyridyl among others.

The phrase "unsubstituted heterocyclylalkyl" refers to unsubstituted alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to a heterocyclyl group as defined above. For example, methyl (-CH₃) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a heterocyclyl group, such as if the carbon of the methyl were bonded to carbon 2 of pyridine (one of the carbons bonded to the N of the pyridine) or carbons 3 or 4 of the pyridine, then the compound is an unsubstituted heterocyclylalkyl group.

The phrase "substituted heterocyclylalkyl" has the same meaning with respect to unsubstituted heterocyclylalkyl groups that substituted aralkyl groups had with respect to unsubstituted aralkyl groups. However, a substituted heterocyclylalkyl group also includes groups in which a non-hydrogen atom is bonded to a heteroatom in the heterocyclyl group of the heterocyclylalkyl group such as, but not limited to, a nitrogen atom in the piperidine ring of a piperidinylalkyl group.

The phrase "unsubstituted alkylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to a nitrogen atom that is bonded to a hydrogen atom and an unsubstituted alkyl group as defined above. For example, methyl (-CH₃) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a nitrogen atom that is bonded to a hydrogen atom and an ethyl group, then the resulting compound is -CH₂-N(H)(CH₂CH₃) which is an unsubstituted alkylaminoalkyl group.

The phrase "substituted alkylaminoalkyl" refers to an unsubstituted alkylaminoalkyl group as defined above except where one or more bonds to a carbon or hydrogen atom in one or both of the alkyl groups is replaced by a bond to a non-carbon or non-hydrogen atom as described above with respect to substituted

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alkyl groups except that the bond to the nitrogen atom in all alkylaminoalkyl groups does not by itself qualify all alkylaminoalkyl groups as being substituted. However, substituted alkylaminoalkyl groups does include groups in which the hydrogen bonded to the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

The phrase "unsubstituted dialkylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon bond or hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to two other similar or different unsubstituted alkyl groups as defined above.

The phrase "substituted dialkylaminoalkyl" refers to an unsubstituted dialkylaminoalkyl group as defined above in which one or more bonds to a carbon or hydrogen atom in one or more of the alkyl groups is replaced by a bond to a non-carbon and non-hydrogen atom as described with respect to substituted alkyl groups. The bond to the nitrogen atom in all dialkylaminoalkyl groups does not by itself qualify all dialkylaminoalkyl groups as being substituted.

The phrase "unsubstituted heterocyclyloxyalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon bond or hydrogen bond is replaced by a bond to an oxygen atom which is bonded to an unsubstituted heterocyclyl group as defined above.

The phrase "substituted heterocyclyloxyalkyl" refers to an unsubstituted heterocyclyloxyalkyl group as defined above in which a bond to a carbon or hydrogen group of the alkyl group of the heterocyclyloxyalkyl group is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups or in which the heterocyclyl group of the

heterocyclyloxyalkyl group is a substituted heterocyclyl group as defined above.

The phrase "unsubstituted arylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon bond or hydrogen bond is replaced

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by a bond to a nitrogen atom which is bonded to at least one unsubstituted aryl group as defined above.

The phrase "substituted arylaminoalkyl" refers to an unsubstituted arylaminoalkyl group as defined above except where either the alkyl group of the arylaminoalkyl group is a substituted alkyl group as defined above or the aryl group of the arylaminoalkyl group is a substituted aryl group except that the bonds to the nitrogen atom in all arylaminoalkyl groups does not by itself qualify all arylaminoalkyl groups as being substituted. However, substituted arylaminoalkyl groups does include groups in which the hydrogen bonded to the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

The phrase "unsubstituted heterocyclylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to at least one unsubstituted heterocyclyl group as defined above.

The phrase "substituted heterocyclylaminoalkyl" refers to unsubstituted heterocyclylaminoalkyl groups as defined above in which the heterocyclyl group is a substituted heterocyclyl group as defined above and/or the alkyl group is a substituted alkyl group as defined above. The bonds to the nitrogen atom in all heterocyclylaminoalkyl groups does not by itself qualify all heterocyclylaminoalkyl groups as being substituted. However, substituted heterocyclylaminoalkyl groups do include groups in which the hydrogen bonded to the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

The phrase "unsubstituted alkylaminoalkoxy" refers to an
unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is
replaced by a bond to an oxygen atom which is bonded to the parent compound and
in which another carbon or hydrogen bond of the unsubstituted alkyl group is
bonded to a nitrogen atom which is bonded to a hydrogen atom and an unsubstituted
alkyl group as defined above.

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The phrase "substituted alkylaminoalkoxy" refers to unsubstituted alkylaminoalkoxy groups as defined above in which a bond to a carbon or hydrogen atom of the alkyl group bonded to the oxygen atom which is bonded to the parent compound is replaced by one or more bonds to a non-carbon and non-hydrogen atoms as discussed above with respect to substituted alkyl groups and/or if the hydrogen bonded to the amino group is bonded to a non-carbon and non-hydrogen atom and/or if the alkyl group bonded to the nitrogen of the amine is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups. The presence of the amine and alkoxy functionality in all alkylaminoalkoxy groups does not by itself qualify all such groups as substituted alkylaminoalkoxy groups.

The phrase "unsubstituted dialkylaminoalkoxy" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to an oxygen atom which is bonded to the parent compound and in which another carbon or hydrogen bond of the unsubstituted alkyl group is bonded to a nitrogen atom which is bonded to two other similar or different unsubstituted alkyl groups as defined above.

The phrase "substituted dialkylaminoalkoxy" refers to an unsubstituted dialkylaminoalkoxy group as defined above in which a bond to a carbon or hydrogen atom of the alkyl group bonded to the oxygen atom which is bonded to the parent compound is replaced by one or more bonds to a non-carbon and non-hydrogen atoms as discussed above with respect to substituted alkyl groups and/or if one or more of the alkyl groups bonded to the nitrogen of the amine is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups. The presence of the amine and alkoxy functionality in all dialkylaminoalkoxy groups does not by itself qualify all such groups as substituted dialkylaminoalkoxy groups.

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The phrase "unsubstituted heterocyclyloxy" refers to a hydroxyl group (-OH) in which the bond to the hydrogen atom is replaced by a bond to a ring atom of an otherwise unsubstituted heterocyclyl group as defined above.

The phrase "substituted heterocyclyloxy" refers to a hydroxyl group

(-OH) in which the bond to the hydrogen atom is replaced by a bond to a ring atom
of an otherwise substituted heterocyclyl group as defined above.

The term "protected" with respect to hydroxyl groups, amine groups, and sulfhydryl groups refers to forms of these functionalities which are protected from undesirable reaction with a protecting group known to those skilled in the art such as those set forth in Protective Groups in Organic Synthesis, Greene, T.W.; Wuts, P. G. M., John Wiley & Sons, New York, NY, (3rd Edition, 1999) which can be added or removed using the procedures set forth therein. Examples of protected hydroxyl groups include, but are not limited to, silyl ethers such as those obtained by reaction of a hydroxyl group with a reagent such as, but not limited to, t-butyldimethyl-chlorosilane, trimethylchlorosilane, triisopropylchlorosilane, triethylchlorosilane; substituted methyl and ethyl ethers such as, but not limited to methoxymethyl ether, methythiomethyl ether, benzyloxymethyl ether, tbutoxymethyl ether, 2-methoxyethoxymethyl ether, tetrahydropyranyl ethers, 1ethoxyethyl ether, allyl ether, benzyl ether; esters such as, but not limited to, benzoylformate, formate, acetate, trichloroacetate, and trifluoracetate. Examples of protected amine groups include, but are not limited to, amides such as, formamide, acetamide, trifluoroacetamide, and benzamide; imides, such as phthalimide, and dithiosuccinimide; and others. Examples of protected sulfhydryl groups include, but are not limited to, thioethers such as S-benzyl thioether, and S-4-picolyl thioether; substituted S-methyl derivatives such as hemithio, dithio and aminothio acetals; and others.

A "pharmaceutically acceptable salt" includes a salt with an inorganic base, organic base, inorganic acid, organic acid, or basic or acidic amino acid. As salts of inorganic bases, the invention includes, for example, alkali metals

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such as sodium or potassium; alkaline earth metals such as calcium and magnesium or aluminum; and ammonia. As salts of organic bases, the invention includes, for example, trimethylamine, triethylamine, pyridine, picoline, ethanolamine, diethanolamine, and triethanolamine. As salts of inorganic acids, the instant invention includes, for example, hydrochloric acid, hydroboric acid, nitric acid, sulfuric acid, and phosphoric acid. As salts of organic acids, the instant invention includes, for example, formic acid, acetic acid, trifluoroacetic acid, fumaric acid, oxalic acid, tartaric acid, maleic acid, citric acid, succinic acid, malic acid, methanesulfonic acid, benzenesulfonic acid, and p-toluenesulfonic acid. As salts of basic amino acids, the instant invention includes, for example, arginine, lysine and ornithine. Acidic amino acids include, for example, aspartic acid and glutamic acid.

Generally, the invention provides compounds including having the structure I. The invention also provides tautomers of the compounds,

pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers. Structure I has the following formula:

$$R^2$$
 R^3
 R^4
 R^9

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Preferred compounds having structure I are those within one of four groups.

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In the first group of compounds:

Y is selected from -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, substituted or unsubstituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups, 15 -NR¹⁶R¹⁷ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted 20 aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted 25 diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, or $-C(=0)R^{18}$ groups;

R⁵, R⁶, R⁷, and R⁸ may be the same or different and are independently selected from H, Cl, Br, F, I, -NO₂, -OH, -OR¹⁹ groups, -NR²⁰R²¹

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groups, -SH, -SR²² groups, -S(=O)R²³ groups, -S(=O)₂R²⁴ groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R²⁵ groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R⁹ and R¹⁴ may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted or unsubstituted dialkylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted alkyl groups, substituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

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-NH(heterocyclyl) groups, -N(heterocyclyl)2 groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl), -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

R¹¹ is selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups,
-N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)
groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups,
-N(aryl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, heterocyclyloxyalkyl
groups, or substituted or unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from substituted or unsubstituted alkyl groups, 15 substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH2, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, 20 substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, 25 -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=0)-O-heterocyclyl groups, -C(=0)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)2 groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted

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or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, or -C(=O)-N(alkyl)(heterocyclyl) groups;

R¹⁵ and R¹⁹ may be the same or different and are independently 5 selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=0)H, -C(=0)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)10 groups, $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups, $-C(=O)N(alkyl)(aryl)_2$ groups, -NH(heterocyclyl) groups, -N(heterocyclyl) groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or 15 unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted 20 (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹⁷ and R²¹ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups,-C(=O)NH₂,

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-C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted 5 alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=0)-heterocyclyl groups, -C(=0)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, $-C(=O)-N(heterocyclyl)_2$ groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted 10 heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted 15 aryloxyalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, or -C(=O)-N(alkyl)(heterocyclyl) groups;

R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted or unsubstituted aryloxy groups, heterocyclyloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, or -N(aryl)O-aryl groups; and

R²² is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

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In other embodiments of the invention, compounds of formula I above include a second group of compounds having the substituents described below:

Y is selected from -OR¹0 groups, -C(=O)-R¹¹ groups, -NR¹²R¹³

5 groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, substituted or unsubstituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

15 R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups, -NR¹⁶R¹ⁿ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted or unsubstituted aminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted or unsubstituted

 R^5 , R^6 , R^7 , and R^8 may be the same or different and are independently selected from H, Cl, Br, F, I, -NO₂, -OH, -OR¹⁹ groups, -NR²⁰R²¹ groups, -SH, -SR²² groups, -S(=O)₂R²³ groups, -S(=O)₂R²⁴ groups, -CN, substituted

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or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R²⁵ groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R⁹ is selected from the group consisting of -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁰ is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(alkyl)₂ groups, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(alkyl)(aryl) groups, -N(aryl)₂ groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(alkyl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

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R¹¹ is selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, substituted or unsubstituted alkyl groups, or substituted or unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from H, substituted or unsubstituted alkyl groups, 10 substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH2, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, 15 -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or 20 unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=0)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups. -C(=O)N(heterocyclyl)2 groups, -C(=O)N(aryl)(heterocyclyl) groups, 25 -C(=O)N(alkyl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

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R¹⁴ is selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁵ and R¹⁹ may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted 10 aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH2, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl)groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted 15 alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted 20 (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups. substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently 25 selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹⁷ and R²¹ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups,

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-C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups. $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups. -C(=0)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, 5 substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups. substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=0)-heterocyclyl groups, -C(=0)-O-heterocyclyl groups. 10 -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)₂ groups, -C(=O)N(aryl)(heterocyclyl) groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups. substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted 15 heterocyclyloxyalkyl groups;

R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted or unsubstituted aryloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(aryl)O-aryl groups; and

 R^{22} is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

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In another embodiment, the present invention provides a third group of compounds having the general formula I above with substituents selected from the following:

Y is selected from -OH, SH, alkylthio groups, arylthio groups, -OR¹⁰ groups, -C(=0)-R¹¹ groups, -NR¹²R¹³ groups, -CN, substituted or unsubstituted 5 alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, 10 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, substituted or 15 unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups. or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups,

-NR¹⁶R¹⁷ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted or unsubstitut

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R⁵, R⁶, R⁷, and R⁸ may be the same or different and are independently selected from H, Cl, Br, F, I, -NO2, -OH, -OR19 groups, -NR20R21 groups, -SH, -SR²² groups, -S(=O)R²³ groups, -S(=O)₂R²⁴ groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R²⁵ groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

 R^9 and R^{14} may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted or unsubstituted dialkylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted alkyl groups, substituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁰ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(alkyl) groups,

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-NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(alkyl)(aryl) groups, -N(aryl)₂ groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

R¹¹ is selected from H, -OH, alkoxy groups, aryloxy groups, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, or substituted or unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl 15 groups, -OH, alkoxy groups, aryloxy groups, -NH2, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted 20 (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=0)H, -C(=0)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, $-C(=O)NH_2$, 25 -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl) groups. -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)N(alkyl)(heterocyclyl) groups. -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted

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heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁵ and R¹⁹ may be the same or different and are independently 5 selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=0)H, -C(=0)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) 10 groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or 15 unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups. substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹⁷ and R²¹ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(alkyl)₂ groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups,

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substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)N(heterocyclyl) groups, -C(=O)N(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)

15 groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, -N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted or unsubstituted heterocyclyl groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(aryl)O-aryl groups; and

 R^{22} is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

In the third group of compounds, at least one of R⁵, R⁶, R⁷, or R⁸ is selected from substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl

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groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or 5 unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups; -OR¹⁹ groups where R¹⁹ is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups. -C(=O)H, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, 10 -C(=O)NH(aryl) groups, $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups. -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl 15 groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted and unsubstituted heterocyclyloxyalkyl groups; -NR²⁰R²¹ groups where R²⁰ is selected from substituted or unsubstituted heterocyclyl groups; -NR²⁰R²¹ groups where R²¹ is selected from substituted or unsubstituted heterocyclyl groups, -C(=0)H, -C(=0)-aryl groups,-C(=0)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl

groups, substituted or unsubstituted hydroxyalkyl groups, substituted or

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unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups; or $-C(=O)R^{25}$ groups where R^{25} is selected from H, $-NH_2$, -NH(alkyl) groups, -NH(aryl) groups, $-N(alkyl)_2$ groups, $-N(aryl)_2$ groups, $-N(alkyl)_3$ groups, $-N(alkyl)_4$ groups, $-N(alkyl)_4$ groups, $-N(alkyl)_4$ groups, $-N(alkyl)_4$ groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aryloxy groups, or substituted or unsubstituted heterocyclyl groups.

In yet another embodiment, the present invention encompasses

compounds of formula I in which the substituents described below define a fourth group of compounds:

Y is selected from -OH, SH, alkylthio groups, arylthio groups, -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, -CN, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkoxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR¹⁴ groups;

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R¹, R², R³, and R⁴ may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO₂, -OH, -OR¹⁵ groups, -NR¹⁶R¹⁷ groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted primary, secondary, or

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tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted or un

R⁵, R⁶, R⁷, and R⁸ may be the same or different and are 10 independently selected from H, Cl, Br, F, I, -NO2, -OH, -OR19 groups, -NR20R21 groups, -SH, -SR²² groups, -S(=0) R^{23} groups, -S(=0) R^{24} groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted 15 or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R²⁵ groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R⁹ and R¹⁴ may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted or unsubstituted dialkylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted alkyl groups, substituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups,

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substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R¹⁰ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH(aryl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -N(alkyl) groups, -N(alkyl) groups, -N(alkyl)2 groups, -N(alkyl)2 groups, -N(alkyl)2 groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

R¹¹ is selected from H, -OH, alkoxy groups, aryloxy groups, -NH₂,
-NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups,
-N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl)
groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, or substituted or
unsubstituted aryl groups;

R¹² is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R¹³ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH₂, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted or unsubstituted arylamino groups, substituted or unsubstituted

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dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)₂ groups, -C(=O)-N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

 R^{15} and R^{19} may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or 15 unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, 20 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted 25 (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁶ and R²⁰ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

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R¹⁷ and R²¹ may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$. -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)₂ groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=0)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, 10 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)₂ groups, -C(=O)-N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups, 15 substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R¹⁸, R²³, R²⁴, and R²⁵ may be the same or different and are

20 independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups,
-N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)
groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,
-N(heterocyclyl)₂ groups, substituted or unsubstituted alkyl groups, substituted or
unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups,

25 substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl
groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-aryl groups;
and

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 R^{22} is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

In the fourth group of compounds, at least one of R¹, R², R³, or R⁴ is an -OR¹⁵ group and R¹⁵ is selected from substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

In the first, second, or third group of compounds Z is preferably an -NR¹⁴ group, more preferably where R¹⁴ is H. Preferred compounds of the fourth group include those compounds in which Z is an -NR¹⁰ group, more preferably where R¹⁰ is H.

Y is preferably an -OR¹⁰ group, an -NR¹²R¹³ group, or a substituted or unsubstituted alkynyl group, or more preferably is an -NR¹²N¹³ group in the first, second, third, and fourth groups of compounds. In more preferred compounds of the first group, Y is a NR¹²R¹³ group and R¹² is H. In more preferred compounds of the second and third groups, Y is a NR¹²R¹³ group and one or both of R¹² and R¹³ are H.

Other preferred compounds of the first, second, and third groups include those where Y is selected from -N(CH₃)₂, -NH(CH₃), -NH(CH₂CH₃), -N(CH₂CH₃)₂, -NH(aryl) groups, -N(aryl)₂ groups, -NHNH₂, -NHN(CH₃)₂, -N(CH₃)NH(CH₃), -NH(CH₂)_mNH₂ groups, -NH(CH₂)_mNH(alkyl) groups, -NH(CH₂)_mNH(alkyl)₂ groups, -N(alkyl)(CH₂)_mNH₂ groups,

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-N(alkyl)(CH₂)_m-NH(alkyl) groups, -N(alkyl)(CH₂)_mN(alkyl)₂ groups,
-NH(CH₂)_n(heterocyclyl) groups, -N(alkyl)[(CH₂)_n(heterocyclyl)] groups,
-NH(CH₂)_mOH groups, -NH(CH₂)_mOCH₃ groups, -NHCH₂CH(NH₂)CH(CH₃)₂,
-NH(2-aminocyclohexyl), -NH(cyclohexyl), -NHOCH₃, -NH(N-morpholinyl),

5 -NH(quinuclidyl), especially -NH(quinuclid-3-yl), or groups where R¹² and R¹³ join to form a substituted or unsubstituted saturated 5 or 6 membered N-containing ring, where m is an integer ranging from 2 to 4 such as 2, 3, or 4 and n is an integer ranging from 0 to 3 such as 0, 1, 2, or 3.

More preferred compounds of the first, second, and third also include those in which Y is selected from -NH(5-benzimidazolyl), -NH(CH₂)₂N(CH₃)₂, -NH(CH₂)₂OH, -NH(CH₂)(4-imidazolyl), -NH(CH₂)(3-imidazolyl), -NH(CH₂)(4-pyridyl), -NH(CH₂)(2-pyridyl), -NH(CH₂)(3-pyridyl), -NH(CH₂)(2-tetrahydrofuranyl), -NH(CH₂)(4-piperidinyl), -NH(CH₂)(3-piperidinyl), -NH(CH₂)₂[2-(N-methylpyrrolidinyl)], -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(CH₂)₂(2-pyrrolidinyl), -NH(3-piperidinyl), or -NH(3-pyrrolidinyl).

Preferred compounds of the first and second groups include those compounds where R¹, R², R³, R⁴, R⁶, R⁷, and R⁸ are all H. Other preferred compounds of the first, second, third, and fourth groups include those where R¹ is 20 selected from H, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocyclyl-, or aryl-aminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted 25 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkyl- or aryl-aminoalkoxy groups, substituted or unsubstituted dialkylaminoalkoxy groups, or substituted or unsubstituted diarylaminoalkoxy groups. Still other compounds of the first, second, third, and fourth groups include those in which R¹ is selected from F, Cl, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups,

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substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocyclyl-, or aryl-aminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or 5 unsubstituted alkylaminoalkoxy groups, substituted or unsubstituted arylaminoalkoxy groups, substituted or unsubstituted dialkylaminoalkoxy groups, substituted or unsubstituted diarylaminoalkoxy groups, or substituted or unsubstituted (alkyl)(aryl)aminoalkoxy groups. Particular examples include: -OCH₃, -OCH₂CH₂(N-morpholinyl), -N-morpholinyl, -N-cis-dialkylmorpholinyl, -N-(4-alkyl)piperazinyl, -OCH2CH2N(alkyl)2 groups, -OCH2CH2NH(alkyl) groups, 10 -OCH2CH2NH2, -OCH2CH2NH(aryl) groups, -OCH2CH2N(aryl)2 groups. -OCH2CH2N(alkyl)(aryl) groups, alkoxy groups, -O(4-piperidinyl), -O[4-(1alkyl)piperidinyl] groups, -O[3-(1-alkyl)piperidinyl] groups, -O[3-quinuclidinyl]. -OCH2(2-pyridyl), -OCH2(4-pyridyl), -O(3-pyrrolidinyl), or -O[3-(1alkyl)pyrrolidinyl] groups. 15

Still other preferred compounds of the first, second, third, and fourth groups include those in which R² is selected from F, Cl, -NO₂, -OCH₃, Nmorpholinyl, -N-cis-dialkylmorpholinyl, -N-(4-alkyl)piperazinyl, or -OCH2(2pyridyl). Other preferred compounds of the first, second, third, and fourth groups include those where R2 is selected from H, F, Cl, -NO2, substituted or unsubstituted 20 heterocyclylalkoxy groups, or substituted or unsubstituted heterocyclyl groups. Yet other preferred compounds of the first, second, third, and fourth groups include those where R2 is selected from F, Cl, -NO2, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocycyl-, and aryl-aminoalkyl groups, substituted or unsubstituted dialkyl- and diarylaminoalkyl groups, substituted or unsubstituted alkylarylaminoalkyl groups, substituted or unsubstituted alkyl- and aryl-aminoalkoxy groups, substituted or unsubstituted dialkyl- and diaryl-aminoalkoxy groups, or substituted or unsubstituted alkylarylaminoalkoxy groups.

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Still further preferred compounds of the first, second, third, and fourth groups include those where R⁶ is an alkyl group having from one to four carbon atoms. In other preferred compounds of the first, second, third, and fourth groups, R⁷ is an alkyl group having from one to four carbon atoms. Still further preferred compounds of the four groups are those in which R⁶ or R⁷ is an -OR¹⁹ group and R¹⁹ is an alkyl group, an aryl group, a heterocyclyl group, or a heterocyclylalkyl group.

In still other preferred compounds of the first, second, third, and fourth groups, R⁶ or R⁷ is a -OCH₂(CH₂)_q(heterocyclyl) group and q is 0, 1, 2, 3, or 4, more preferably where the heterocyclyl group of the -OCH₂(CH₂)₉(heterocyclyl) group is a heterocycle selected from substituted or unsubstituted morpholine, substituted or unsubstituted piperazine, substituted or unsubstituted piperidine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted furan. substituted or unsubstituted thiophene, substituted or unsubstituted tetrahydrofuran, substituted or unsubstituted tetrahydrothiophene, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzothiazole.

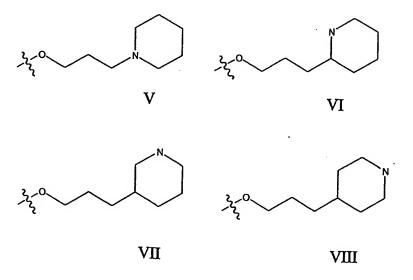
In groups including heterocyclyl groups, the heterocyclyl may be attached in various ways. For example, in the -OCH₂(CH₂)_q(heterocyclyl) group, the heterocyclyl group may be bonded to a methylene carbon of the -OCH₂(CH₂)_q group of the -OCH₂(CH₂)_q(heterocyclyl) through various ring members. By way of non-limiting example, where q is 1 and the heterocyclyl group is tetrahydrofuran,

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the group could be represented by the formula -OCH₂CH₂(tetrahydrofuranyl) which corresponds to the following two structures:

where structure III represents the group that can be referred to as the -OCH₂CH₂(2tetrahydrofuranyl) group and structure IV represents the group that can be referred to as the -OCH₂CH₂(3-tetrahydrofuranyl) group. When the heterocyclyl group is a N-containing heterocycle, such as, but not limited to piperidine, piperazine, morpholine, or pyrrolidine, the heterocycle can be bonded to the methylene carbon through a ring carbon atom or through a nitrogen atom in the ring of the Ncontaining heterocycle. Both of these are preferred. Where the heterocyclyl group is a piperidine and q is 2 for an -OCH₂(CH₂)_q(heterocyclyl) group, the following structures are possible and preferred:



Structure V is an example of a -O(CH₂)₃(N-piperidinyl) or -O(CH₂)₃(1-piperidinyl) group. Structure VI is an example of a -O(CH₂)₃-(2-piperidinyl) group. Structure VII is an example of a -O(CH₂)₃(3-piperidinyl)

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group. Structure VIII is an example of a -O(CH₂)₃(4-piperidinyl) group. Where the heterocyclyl group is a piperazine and q is 1 for an -OCH₂(CH₂)₄(heterocyclyl) group, the following structures are possible and preferred:

Structure IX is an example of a -O(CH₂)₂(2-piperazinyl) group, and structure X is an example of a -O(CH₂)₂(1-piperazinyl) or -O(CH₂)₂(N-piperazinyl) group. Where the heterocyclyl group is a morpholine and q is 1 for an -OCH₂(CH₂)_q(heterocyclyl) group, the following structures are possible and preferred:

Structure XI is an example of a -O(CH₂)₂(3-morpholinyl) group, structure XII is an example of a -O(CH₂)₂(4-morpholinyl) or -O(CH₂)₂(N-morpholinyl) group, and structure XIII is an example of a -O(CH₂)₂(2-morpholinyl) group. It will be observed that where the group is a pyrrolidine, and q is 1, the structures available include -O(CH₂)₂(1-pyrrolidinyl) or -O(CH₂)₂(N-pyrrolidinyl), -O(CH₂)₂(2-pyrrolidinyl), and -O(CH₂)₂(3-pyrrolidinyl).

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Yet other preferred compounds of the first, second, third, and fourth groups include those where at least one of R⁵, R⁶, R⁷, and R⁸ is a substituted or unsubstituted heterocyclyl group, more specifically a substituted or unsubstituted heterocyclyl group comprising at least one O or N atom, still more particularly a substituted or unsubstituted heterocyclyl group selected from morpholine, piperazine, piperidine, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyrrolidine, pyrazole, pyrrole, thiomorpholine, thiomorpholine in which the S atom of the thiomorpholine group is bonded to one or more O atoms, homopiperazine, benzimidazole, oxazolidin-2-one, pyrrolidin-2-one, imidazole, isoxazole, oxazole, isothiazole, thiazole, thiophene, furan, pyran, tetrahydrothiophene, tetrahydrofuran, tetrahydropyran, or pyridine.

Other preferred compounds of the first, second, third, and fourth groups include those in which at least one of R¹⁹ or R²¹ is selected from substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or 15 unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, (alkyl)(aryl)aminoalkyl groups, or substituted or unsubstituted heterocyclylalkyl groups, including: -CH2(CH2)pNH2 groups, -CH2(CH2) $_p$ NH(alkyl) groups, -CH2(CH2) $_p$ NH(aryl) groups, -CH2(CH2) $_p$ N(alkyl) $_2$ groups, -CH2(CH2) $_p$ N(aryl) $_2$ groups, -CH2(CH2) $_p$ N(alkyl)(aryl) groups, or 20 -CH2(CH2)p(heterocyclyl) groups, wherein p is an integer ranging from 0 to 4 and the heterocyclyl group of the -CH2(CH2)p(heterocyclyl) group is a N-containing heterocycle selected from substituted or unsubstituted morpholine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted piperazine, substituted or unsubstituted piperidine, substituted or unsubstituted pyrrole, substituted or 25 unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, 30 substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole,

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substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzothiazole.

Still further preferred compounds according to the first, second. third, and fourth groups include those in which R²⁵ is selected from substituted or 5 unsubstituted aryl groups, substituted or unsubstituted alkyl groups, -NH₂, -NH(alkyl) groups, -N(alkyl)2 groups, -NH(aryl) groups, -N(aryl)2 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, -N(heterocyclyl)₂ groups, or N-containing 10 heterocycles. In such compounds, the N-containing heterocycles are bonded to the carbonyl carbon of the -C(=O)-R²⁵ group through either a nitrogen atom or a carbon atom in the rings of the N-containing heterocycles. In more preferred such compounds that are provided, the N-containing heterocycle of the R²⁵ group is selected from substituted or unsubstituted morpholine, substituted or unsubstituted 15 pyrrolidine, substituted or unsubstituted piperazine, substituted or unsubstituted piperidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted 20 homopiperazine, substituted or unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or 25 substituted or unsubstituted benzothiazole.

Preferred compounds according to the first, third, and fourth groups of compounds are also those where R⁹ is H.

Preferred compounds of the fourth group of compounds include those where R¹ is an -OR¹⁵ group and R¹⁵ is selected from substituted or unsubstituted

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heterocyclylalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups.

Other particularly preferred inhibitors of VEGF-RTK are compounds having the structure II, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers.

Structure II has the following formula:

 \mathbf{II}

In compounds having structure II, Y is selected from H, -OH, -OR¹⁰ groups, -SH, -SR¹¹ groups, -NR¹²R¹³ groups, -CN, -C(=O)-R¹⁴ groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted or un

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unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups.

In preferred compounds of structure II, Y is selected from H. -OH. -OR9 groups, or -NR11R12 groups. More preferably, Y is a -NR11R12 group. Still more preferably, Y is a -NR¹¹R¹² group and both R¹¹ and R¹² are hydrogen. In 10 other preferred compounds having the structure II, Y is selected from -N(CH₃)₂. -NH(CH₃), -NH(CH₂CH₃), -N(CH₂CH₃)₂, -NH(aryl) groups, -N(aryl)₂ groups -NHNH2, -NHN(CH3)2, -N(CH3)NH(CH3), -NH(CH2)mNH2 groups, -NH(CH2)mNH(alkyl) groups, -NH(CH2)mN(alkyl)2 groups, -N(alkyl)(CH2)mNH2 groups, -N(alkyl)(CH₂)_mNH(alkyl) groups, -N(alkyl)(CH₂)_mN(alkyl)₂ groups, 15 -NH(CH₂)_n(heterocyclyl) groups, -N(alkyl)[(CH₂)_n(heterocyclyl)] groups, -NH(CH₂)_mOH groups, -NH(CH₂)_mOCH₃ groups, -NHCH₂CH(NH₂)CH(CH₃)₂, -NH(2-aminocyclohexyl), -NH(cyclohexyl), -NHOCH₃, -NH(N-morpholinyl), -NH(quinuclidyl), especially -NH(quinuclid-3-yl), and groups where R¹¹ and R¹² join to form a substituted or unsubstituted saturated 5 or 6 membered N-containing 20 ring, where m is 2, 3, or 4 and n is 0, 1, 2, or 3. Still more preferred compounds of this type are those in which Y is selected from -NH(5-benzimidazolyl), -NH(CH₂)₂N(CH₃)₂, -NH(CH₂)₂OH, -NH(CH₂)(4-imidazolyl), -NH(CH₂)(3imidazolyl), -NH(CH₂)(4-pyridyl), -NH(CH₂)(2-pyridyl), -NH(CH₂)(3-pyridyl). -NH(CH₂)(2-tetrahydrofuranyl), -NH(CH₂)(4-piperidinyl), -NH(CH₂)(3-25 piperidinyl), -NH(CH₂)₂[2-(N-methyl-pyrrolidinyl)], -NH(CH₂)₂(2-pyrrolidinyl). -NH(CH₂)[2-(N-methylpyrrolidinyl)], -NH(CH₂)(2-pyrrolidinyl), -NH(3piperidinyl), or -NH(3-pyrrolidinyl).

In compounds of structure II, X¹, X², X³, and X⁴ are selected from C or N and at least one of X¹, X², X³, and X⁴ is N. In some preferred compounds of structure II, X¹ is N, R⁵ is absent or H, and X², X³, and X⁴ are all C. In other

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preferred compounds of structure II, X^2 is N, R^6 is absent or H, and X^1 , X^3 , and X^4 are C. In other preferred compounds of structure II, X^3 is N, R^7 is absent or H, and X^1 , X^2 , and X^4 are all C. In still other preferred compounds of structure II, X^4 is N, R^8 is absent or H, and X^1 , X^2 , and X^3 are all C.

In compounds of structure II, R1, R2, R3, R4, R5, R6, R7, and R8 may 5 be the same or different and are independently selected from H, Cl, Br, F, I, -NO2, -CN, -OH, -OR15 groups, -NR16R17 groups, -C(=O)R18 groups, -SH, -SR19 groups, -S(=O)R²⁰ groups, S(=O)₂R²¹ groups, substituted or unsubstituted amidinyl groups. substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, 10 secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted 15 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted 20 aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups. In compounds of structure II, R5 is absent or is H if X1 is N, R6 is absent or is H if X2 is N, R⁷ is absent or is H if X³ is N, and R⁸ is absent or is H if X⁴ is N.

Some preferred compounds have the structure II where at least one of R¹, R², R³, R⁴, R⁵, R⁶, R⁷, or R⁸ is a substituted or unsubstituted heterocyclyl group, and, in more particular embodiments, a substituted or unsubstituted heterocyclyl group selected from morpholine, piperazine, piperidine, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyrrolidine, pyrazole, pyrrole, thiomorpholine, homopiperazine, benzimidazole, oxazolidin-2-one, pyrrolidin-2-one, imidazole, isoxazole, oxazole, isothiazole, thiazole, thiophene, furan, pyran, tetrahydrothiophene, tetrahydrofuran, tetrahydropyran, and pyridine.

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Still other preferred compounds having structure Π are those in which R¹, R², R³, and R⁴ are H. In some preferred embodiments, R¹ is selected from H, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, 5 substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylheterocyclyl-, or aryl-aminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkyl- or aryl-aminoalkoxy groups, substituted or unsubstituted 10 dialkylaminoalkoxy groups, or substituted or unsubstituted diarylaminoalkoxy groups. In other preferred compounds, R1 is selected from F, Cl, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups. substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocyclyl-, or aryl-aminoalkyl groups, substituted or unsubstituted 15 dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylaminoalkoxy groups, substituted or unsubstituted arylaminoalkoxy groups, substituted or unsubstituted dialkylaminoalkoxy groups, substituted or unsubstituted diarylaminoalkoxy groups, or substituted or unsubstituted (alkyl)(aryl)aminoalkoxy groups. Particular examples include: -OCH₃, -OCH₂CH₂(N-morpholinyl), -N-morpholinyl, -N-cis-dimethylmorpholinyl, -N-(4-alkyl)piperazinyl, -OCH2CH2N(alkyl)2 groups, -OCH2CH2NH(alkyl) groups, -OCH₂CH₂NH₂, -OCH₂CH₂NH(aryl) groups, -OCH₂CH₂N(aryl)₂ groups, alkoxy groups, -OCH2CH2N(alkyl)(aryl) groups, -O(4-piperidinyl), -O[4-(1alkyl)piperidinyl] groups, -O[3-(1-alkyl)piperidinyl] groups, -O[3-quinuclidinyl], -OCH₂(2-pyridyl), -OCH₂(4-pyridyl), -O(3-pyrrolidinyl), -O[3-(1alkyl)pyrrolidinyl], or other -O(heterocyclyl) groups not listed in this paragraph.

In other compounds having the structure II, R² is selected from F, Cl, -NO₂, -OCH₃, -N-morpholinyl, -N-cis-dialkylmorpholinyl, -N-(4alkyl)piperazinyl, or -OCH2(2-pyridyl). In yet other compounds having the 30 structure II, R² is selected from H, F, Cl, -NO₂, substituted or unsubstituted

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heterocyclylalkoxy groups, or substituted or unsubstituted heterocyclyl groups. Yet other preferred compounds having the structure II include those where R² is selected from F, Cl, -NO₂, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocycyl-, and aryl-aminoalkyl groups, substituted or unsubstituted dialkyl- and diaryl-aminoalkyl groups, substituted or unsubstituted alkylarylaminoalkyl groups, substituted or unsubstituted alkylarylaminoalkyl groups, substituted or unsubstituted alkyl- and diaryl-aminoalkoxy groups, or substituted or unsubstituted alkylarylaminoalkoxy groups.

10 In some preferred compounds having structure II, at least two of X1, X², X³, and X⁴ are C and the corresponding substituents R⁵, R⁶, R⁷, and R⁸ are hydrogen, and at least one of X1, X2, X3, and X4 is N. In yet other preferred compounds having structure II, three of R5, R6, R7, and R8 are hydrogen and one of X¹, X², X³, and X⁴ is N. In still other more preferred compounds of structure II, R⁶, R⁷, or both R⁶ and R⁷ are alkyl groups such as those having from one to four carbon atoms. In yet other preferred compounds of structure II, R⁶ or R⁷ is an -OR14 group and R14 is an alkyl, aryl, heterocyclyl, or heterocyclylalkyl group. In still further compounds of structure II, R⁶ or R⁷ is a -OCH₂(CH₂)_q(heterocyclyl) group and q is 0, 1, 2, 3, or 4. In more preferred compounds in which R⁶ or R⁷ is 20 a -OCH2(CH2)q-(heterocyclyl) group, the heterocyclyl group of the -OCH2(CH2)n(heterocyclyl) group is a heterocycle selected from substituted or unsubstituted morpholine, substituted or unsubstituted piperazine, substituted or unsubstituted piperidine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or 25 unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted thiomorpholine in which the S atom of the thiomorpholine group is bonded to one or more O atoms, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-30 2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted

pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted

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isoxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted furan, substituted or unsubstituted thiophene, substituted or unsubstituted tetrahydrofuran, substituted or unsubstituted tetrahydrothiophene, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzothiazole.

In compounds of structure II, R^9 is selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH₂, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups. One group of particularly preferred compounds of structure II are those in which R^9 is hydrogen.

In compounds of structure II, R¹⁰ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(alkyl)2 groups, -N(alkyl)2 groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)2 groups, -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

In compounds of structure II, R¹¹ and R¹⁹ may be the same or

different and are independently selected from substituted or unsubstituted alkyl
groups, or substituted or unsubstituted aryl groups whereas R¹² is selected from H,
substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups,
or substituted or unsubstituted heterocyclyl groups.

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In compounds of structure II, R13 is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH2, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted 5 aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted 10 diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH₂, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) 15 groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)₂ groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted 20 heterocyclyloxyalkyl groups. R¹² and R¹³ may join together to form a 5 to 7 membered saturated or unsaturated, substituted or unsubstituted N-containing ring.

In compounds of structure II, R¹⁴ is selected from H, -OH, alkoxy groups, aryloxy groups, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)₂ groups, -N(alkyl)(heterocyclyl) groups, or -N(aryl)(heterocyclyl) groups.

In compounds of structure II, R¹⁵ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or

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unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)₂ groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted 5 aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted 10 diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, or substituted or unsubstituted 15 heterocyclyloxyalkyl groups.

In compounds of structure II, R¹⁶ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups whereas R¹⁷ is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or 20 unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted 25 or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (aryl)(alkyl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-Oheterocyclyl groups, -C(=O)NH(heterocyclyl) groups, $-C(=O)N(heterocyclyl)_2$ groups, -C(=O)-N(alkyl)(heterocyclyl) groups,

-C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted

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heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted heterocyclyloxyalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, or -NH2 groups. R¹⁶ and R¹⁷ may join together to form a 5 to 7 membered saturated or unsaturated, substituted or unsubstituted N-containing ring.

Finally, in compounds of structure II, R¹⁸, R²⁰, and R²¹ may be the same or different and are independently selected from H, -NH₂, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)₂ groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups.

15 Compounds having the structure II may include those in which R¹⁸ is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -NH2, -NH(alkyl) groups, -N(alkyl)2 groups, -NH(aryl) groups, -N(aryl)₂ groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, -N(heterocyclyl)2 groups, or N-containing heterocycles, and the N-containing heterocycles are bonded 20 to the carbonyl carbon of the -C(=O)-R¹⁸ group through either a nitrogen atom or a carbon atom in the rings of the N-containing heterocycles. In still more preferred compounds in which R18 is a N-containing heterocycle, the N-containing heterocycle of the R¹⁸ group is selected from substituted or unsubstituted morpholine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted piperazine, 25 substituted or unsubstituted piperidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted 30 thiomorpholine, substituted or unsubstituted homopiperazine, substituted or

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unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzoxazole.

Other preferred compounds having structure II are provided in which R¹⁵ or R¹⁷ is selected from substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted 10 arylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, or substituted or unsubstituted heterocyclylaminoalkyl groups including: -CH₂(CH₂)_pNH₂ groups, -CH₂(CH₂)_pNH(alkyl) groups, -CH₂(CH₂)_pNH(aryl) groups, -CH₂(CH₂)_pN(alkyl)₂ 15 groups, -CH2(CH2), N(aryl)2 groups, -CH2(CH2), N(alkyl)(aryl) groups, or -CH₂(CH₂)_p(heterocyclyl) groups, where p is an integer ranging from 0 to 4 and the heterocyclyl group of the -CH₂(CH₂)_p(heterocyclyl) group is a N-containing heterocycle selected from substituted or unsubstituted morpholine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted piperazine, substituted or 20 unsubstituted piperidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-2-one, 25 substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzothiazole.

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Compounds of structure I are readily synthesized from simple starting molecules as shown in the following Examples. Compounds of structure I may generally be prepared using benzene substituted with nitrile or carboxylic acid groups in addition to other optional groups.

Compounds of structure I may be synthesized from simple starting molecules as shown in Schemes 1-4 and exemplified in the Examples. As shown in Scheme 1, compounds of structure I may generally be prepared using aromatic compounds substituted with amines and carboxylic acid groups.

Scheme 1.

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As shown in Scheme 1, a substituted aromatic compound such as a substituted or unsubstituted 2-aminobenzoic acid may be reacted with an acyl halide such as methyl 2-(chlorocarbonyl)acetate to produce an amide that will react with a substituted or unsubstituted 1,2-diaminobenzene. The resulting product is a 4-hydroxy-substituted compound of structure I. One skilled in the art will recognize that the procedure set forth in Scheme 1 may be modified to produce various compounds.

A method for preparing 4-amino substituted compounds of structure I is shown in Scheme 2. As shown in Scheme 2, aromatic compounds substituted with amine and nitrile groups may be used to synthesize 4-amino substituted compounds of structure I. A compound such as ethyl 2-cyanoacetate may be

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reacted with ethanol to produce ethyl 3-ethoxy-3-iminopropanoate hydrochloride. Subsequent reaction with a substituted or unsubstituted 1,2-phenylenediamine provides substituted or unsubstituted ethyl 2-benzimidazol-2-ylacetate. Reaction of a substituted or unsubstituted ethyl 2-benzimidazol-2-ylacetate with an aromatic compound having an amine and nitrile group such as substituted or unsubstituted 2-aminobenzonitrile with a base such as lithium bis(trimethylsilyl)amide or a Lewis acid such as tin tetrachloride provides the substituted or unsubstituted 4-amino substituted compound of structure I.

Scheme 3 illustrates a general synthetic route that allows for the synthesis of 4-dialkylamino and 4-alkylamino compounds of structure I. An inspection of Scheme 3 shows that 4-hydroxy substituted compounds of structure I may be converted into the 4-chloro derivative by reaction with phosphorous oxychloride or thionyl chloride. The 4-chloro derivative may then be reacted with an alkylamine or dialkylamine to produce the corresponding 4-alkylamino or 4-dialkylamino derivative. Deprotection affords the final 4-alkylamino or 4-dialkylamino compounds of structure I. Other groups that may be reacted with the 4-chloro derivative in this manner include, but are not limited to, ROH, RSH, and CuCN.

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As shown in Scheme 4, the synthesis of compounds of structure I having a H, alkyl group, aryl group, or heterocyclyl group in the 4-position may be accomplished using a substituted or unsubstituted 2-benzimidazol-2-ylacetate prepared as shown in Schemes 2 and 3.

Heteroaromatic diamines may be used as precursors of compounds of structure II. The synthesis of compounds of structure II where $Y = NH_2$ is depicted in Scheme 5.

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Scheme 5.

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A compound such as ethyl cyanoacetate may be condensed with a substituted or unsubstituted heterocycle containing two ortho amino groups such as substituted or unsubstituted 1,2-diaminopyridine to obtain a substituted or unsubstituted 2-imidazolo[5,4-b]pyridin-2-ylethanenitrile, which may subsequently be hydrolyzed in acidic medium to provide a substituted or unsubstituted ethyl 2-imidazolo[5,4-b]pyridin-2-ylacetate. As an alternate route, a substituted or unsubstituted ethyl 2-imidazolo[5,4-b]pyridin-2-ylacetate may be obtained from a compound such as the hydrochloride salt of 3-ethoxy-3-iminopropanoate and a substituted or unsubstituted 1,2-diaminopyridine. Reaction of a substituted or unsubstituted ethyl 2-imidazolo[5,4-b]pyridin-2-ylacetates with an aromatic compound having an amine and nitrile group such as substituted or unsubstituted 2-aminobenzonitrile with a base such as lithium bis(trimethylsilyl)amide provides the substituted or unsubstituted compound of structure II.

The instant invention also provides for compositions which may be prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers thereof, with pharmaceutically acceptable carriers, excipients, binders, diluents or the like, to treat or ameliorate a variety of disorders related to the activity of VEGF-RTK, more particularly angiogenesis associated with cancer. A therapeutically effective dose further refers to that amount of one or more compounds of the instant invention sufficient to result

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in amelioration of symptoms of the disorder. The pharmaceutical compositions of the instant invention can be manufactured by methods well known in the art such as conventional granulating, mixing, dissolving, encapsulating, lyophilizing, emulsifying or levigating processes, among others. The compositions can be in the form of, for example, granules, powders, tablets, capsules, syrup, suppositories, injections, emulsions, elixirs, suspensions or solutions. The instant compositions can be formulated for various routes of administration, for example, by oral administration, by transmucosal administration, by rectal administration, or subcutaneous administration as well as intrathecal, intravenous, intramuscular, intraperitoneal, intranasal, intraocular or intraventricular injection. The compound or compounds of the instant invention can also be administered in a local rather than a systemic fashion, such as injection as a sustained release formulation. The following dosage forms are given by way of example and should not be construed as limiting the instant invention.

15 For oral, buccal, and sublingual administration, powders, suspensions, granules, tablets, pills, capsules, gelcaps, and caplets are acceptable as solid dosage forms. These can be prepared, for example, by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers thereof, with at least one additive or excipient such as a starch or other additive. Suitable additives or excipients are sucrose, lactose, cellulose sugar, mannitol, maltitol, dextran, 20 sorbitol, starch, agar, alginates, chitins, chitosans, pectins, tragacanth gum, gum arabic, gelatins, collagens, casein, albumin, synthetic or semi-synthetic polymers or glycerides, methyl cellulose, hydroxypropylmethyl-cellulose, and/or polyvinylpyrrolidone. Optionally, oral dosage forms can contain other ingredients to 25 aid in administration, such as an inactive diluent, or lubricants such as magnesium stearate, or preservatives such as paraben or sorbic acid, or anti-oxidants such as ascorbic acid, tocopherol or cysteine, a disintegrating agent, binders, thickeners, buffers, sweeteners, flavoring agents or perfuming agents. Additionally, dyestuffs or pigments may be added for identification. Tablets and pills may be further treated with suitable coating materials known in the art. 30

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Liquid dosage forms for oral administration may be in the form of pharmaceutically acceptable emulsions, syrups, elixirs, suspensions, slurries and solutions, which may contain an inactive diluent, such as water. Pharmaceutical formulations may be prepared as liquid suspensions or solutions using a sterile liquid, such as, but not limited to, an oil, water, an alcohol, and combinations of these. Pharmaceutically suitable surfactants, suspending agents, emulsifying agents, may be added for oral or parenteral administration.

As noted above, suspensions may include oils. Such oil include, but are not limited to, peanut oil, sesame oil, cottonseed oil, corn oil and olive oil. Suspension preparation may also contain esters of fatty acids such as ethyl oleate, isopropyl myristate, fatty acid glycerides and acetylated fatty acid glycerides. Suspension formulations may include alcohols, such as, but not limited to, ethanol, isopropyl alcohol, hexadecyl alcohol, glycerol and propylene glycol. Ethers, such as but not limited to, poly(ethyleneglycol), petroleum hydrocarbons such as mineral oil and petrolatum; and water may also be used in suspension formulations.

For nasal administration, the pharmaceutical formulations may be a spray or aerosol containing and appropriate solvents and optionally other compounds such as, but not limited to, stabilizers, antimicrobial agents, antioxidants, pH modifiers, surfactants, bioavailability modifiers and combinations of these. A propellant for an aerosol formulation may include compressed air, nitrogen, carbon dioxide, or a hydrocarbon based low boiling solvent. The compound or compounds of the instant invention are conveniently delivered in the form of an aerosol spray presentation from a nebulizer or the like.

Injectable dosage forms generally include aqueous suspensions or oil suspensions which may be prepared using a suitable dispersant or wetting agent and a suspending agent. Injectable forms may be in solution phase or in the form of a suspension, which is prepared with a solvent or diluent. Acceptable solvents or vehicles include sterilized water, Ringer's solution, or an isotonic aqueous saline solution. Alternatively, sterile oils may be employed as solvents or suspending

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For injection, the pharmaceutical formulation may be a powder

agents. Preferably, the oil or fatty acid is non-volatile, including natural or synthetic oils, fatty acids, mono-, di- or tri-glycerides.

suitable for reconstitution with an appropriate solution as described above.

5 Examples of these include, but are not limited to, freeze dried, rotary dried or spray dried powders, amorphous powders, granules, precipitates, or particulates. For injection, the formulations may optionally contain stabilizers, pH modifiers, surfactants, bioavailability modifiers and combinations of these. The compounds may be formulated for parenteral administration by injection such as by bolus injection or continuous infusion. A unit dosage form for injection may be in ampoules or in multi-dose containers.

For rectal administration, the pharmaceutical formulations may be in the form of a suppository, an ointment, an enema, a tablet or a cream for release of compound in the intestines, sigmoid flexure and/or rectum. Rectal suppositories are prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers of the compound, with acceptable vehicles, for example, cocoa butter or polyethylene glycol, which is present in a solid phase at normal storing temperatures, and present in a liquid phase at those temperatures suitable to release a drug inside the body, such as in the rectum. Oils may also be employed in the preparation of formulations of the soft gelatin type and suppositories. Water, saline, aqueous dextrose and related sugar solutions, and glycerols may be employed in the preparation of suspension formulations which may also contain suspending agents such as pectins, carbomers, methyl cellulose, hydroxypropyl cellulose or carboxymethyl cellulose, as well as buffers and preservatives.

Besides those representative dosage forms described above, pharmaceutically acceptable excipients and carries are generally known to those skilled in the art and are thus included in the instant invention. Such excipients and

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carriers are described, for example, in "Remingtons Pharmaceutical Sciences" Mack Pub. Co., New Jersey (1991), which is incorporated herein by reference.

The formulations of the invention may be designed for to be short-acting, fast-releasing, long-acting, and sustained-releasing as described below.

Thus, the pharmaceutical formulations may also be formulated for controlled release or for slow release.

The instant compositions may also comprise, for example, micelles or liposomes, or some other encapsulated form, or may be administered in an extended release form to provide a prolonged storage and/or delivery effect.

Therefore, the pharmaceutical formulations may be compressed into pellets or cylinders and implanted intramuscularly or subcutaneously as depot injections or as implants such as stents. Such implants may employ known inert materials such as silicones and biodegradable polymers.

Specific dosages may be adjusted depending on conditions of disease, the age, body weight, general health conditions, sex, and diet of the subject, dose intervals, administration routes, excretion rate, and combinations of drugs. Any of the above dosage forms containing effective amounts are well within the bounds of routine experimentation and therefore, well within the scope of the instant invention.

A therapeutically effective dose may vary depending upon the route of administration and dosage form. The preferred compound or compounds of the instant invention is a formulation that exhibits a high therapeutic index. The therapeutic index is the dose ratio between toxic and therapeutic effects which can be expressed as the ratio between LD50 and ED50. The LD50 is the dose lethal to 50% of the population and the ED50 is the dose therapeutically effective in 50% of the population. The LD50 and ED50 are determined by standard pharmaceutical procedures in animal cell cultures or experimental animals.

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"Treating" within the context of the instant invention, means an alleviation of symptoms associated with a disorder or disease, or halt of further progression or worsening of those symptoms, or prevention or prophylaxis of the disease or disorder. For example, within the context of treating patients in need of an inhibitor of VEGF-RTK, successful treatment may include a reduction in the proliferation of capillaries feeding a tumor or diseased tissue, an alleviation of symptoms related to a cancerous growth or tumor, proliferation of capillaries, or diseased tissue, a halting in capillary proliferation, or a halting in the progression of a disease such as cancer or in the growth of cancerous cells. Treatment may also include administering the pharmaceutical formulations of the present invention in combination with other therapies. For example, the compounds and pharmaceutical formulations of the present invention may be administered before, during, or after surgical procedure and/or radiation therapy. The compounds of the invention can also be administered in conjunction with other anti-cancer drugs including those used in antisense and gene therapy.

A method of treating a patient in need of an inhibitor of vascular endothelial growth factor receptor tyrosine kinase includes administering an effective amount of a pharmaceutical formulation according to the invention to a patient in need thereof.

A method for inhibiting tumor growth in a patient includes administering an effective amount of the compound or a pharmaceutically acceptable salt thereof to a patient having a tumor.

A method for inhibiting the proliferation of capillaries in a patient includes administering an effective amount of the compound or a pharmaceutically acceptable salt thereof according to a patient in need.

A method of preparing pharmaceutical formulations includes mixing any of the above-described compounds with a pharmaceutically acceptable carrier and water or an aqueous solution.

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The present invention, thus generally described, will be understood more readily by reference to the following examples, which are provided by way of illustration and are not intended to be limiting of the present invention.

EXAMPLES

5 The following abbreviations are used in the Examples:

ATP: Adenosine triphosphate
BSA: Bovine Serum Albumin
DMA: N,N-Dimethylacetamide
DMF: N,N-Dimethylformamide

10 dppf: 1,1'(diphenylphosphino)ferrocene

DTT: DL-Dithiothreitol

EDTA: Ethylene diamine tetraacetic acid

EtOAc: Ethyl acetate

EtOH: Ethanol

15 HBTU: O-Benzotriazol-1-yl-N,N,N',N'-tetramethyluronium

hexafluorophosphate

IC₅₀ value: The concentration of an inhibitor that causes a 50 % reduction

in a measured activity.

LiHMDS: Lithium bis(trimethylsilyl)amide

20 MeOH: Methanol

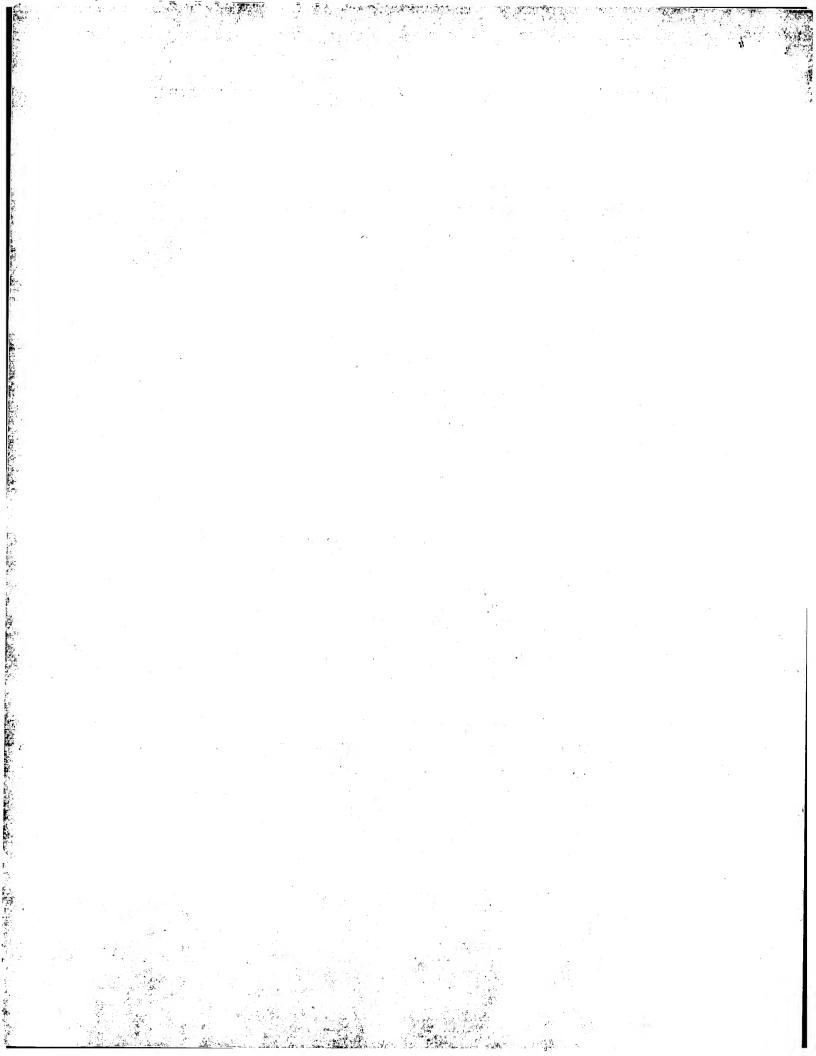
NMP: N-methylpyrrolidone

THF: Tetrahydrofuran

The compounds were named using Nomenclator (v. 3.0 & v. 5.0)

25 from CmemInovation Software, Inc. and ACD/Name v. 4.53.

The various aryl diamine starting materials used to synthesize benzimidazole acetates may be obtained from commercial sources, prepared by methods know to one of skill in the art, or prepared by the following general Methods 1-15.



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Method 1

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2,4-Difluoronitrobenzene (1.0 eq) was placed in a dry round-bottomed flask equipped with a dry ice condenser charged with acetone and dry ice.
5 Ammonia was condensed into the flask and the resulting solution was stirred at reflux for 7 hours. A yellow precipitate formed within 1 hour. After 7 hours, the condenser was removed and the liquid ammonia was allowed to evaporate over several hours. The crude product was purified by flash chromatography on silica gel (85:15 hexanes:ethyl acetate, product at R_f = 0.32, contaminant at R_f = 0.51);
10 GC/MS m/z 156.1 (M+), R_f 11.16 minutes.

The resulting 5-fluoro-2-nitrophenylamine (1.0 eq) and an amine (1.1 eq) e.g. N-methyl piperazine, were dissolved in NMP and triethylamine (2.0 eq) was added. The reaction mixture was heated at 100°C for 3 hours. The solution was then cooled to room temperature and diluted with water. The resulting precipitate was filtered and dried under vacuum to provide the 2-nitro-diamino product. Alternatively, the same product may be obtained from commercially available 5-chloro-2-nitrophenylamine under identical conditions except heating at 130°C for 1-2 days. In some examples, the displacement on either 5-fluoro-2-nitrophenylamine or 5-chloro-2-nitrophenylamine can be conducted in neat amine (5 eq) at 100°C or 130 °C, respectively. The product is isolated in an identical manner. LC/MS m/z 237.1 (MH+), Rt 1.304 minutes.

The nitroamine (1.0 eq) and 10% Pd/C (0.1 eq) was suspended in anhydrous ethanol at room temperature. The reaction flask was evacuated and subsequently filled with H₂. The resulting mixture was then stirred under a hydrogen atmosphere overnight. The resulting solution was filtered through Celite and concentrated under vacuum to provide the crude product which was used without further purification.

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Method 2

A round-bottom flask was charged with 2,3-difluoro-6-nitrophenylamine (1 eq) and enough NMP to make a viscous slurry. An amine (5 eq), e.g. N-methyl piperazine, was added and the solution was heated at 100°C. After 2 hours, the solution was cooled and poured into water. A bright yellow solid formed which was filtered and dried. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS m/z 225.1 (MH+), R₁0.335 minutes.

10 Method 3

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To a 0.1 M DMF solution of 1,3-difluoro-2-nitrobenzene was added Et₃N (2 eq) followed by an amine (1 eq), e.g. morpholine. The mixture was stirred for 18 hours and then diluted with water and extracted with ethyl acetate. LC/MS m/z 227.2 (MH+), R₂.522 minutes. The combined organic layers were dried over MgSO₄, filtered, and concentrated. Ammonia was condensed into a bomb containing the crude product. The bomb was sealed and heated to 100°C (over 400 psi). After 72 hours the bomb was allowed to cool and the ammonia was evaporated to provide a reddish solid. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS m/z 194.1 (MH+), R₂1.199 minutes.

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Method 4

$$NH_2$$
 NO_2
 RO
 NH_2
 NH_2
 NH_2

To a stirred NMP solution containing NaH (1.3 eq) was added an alcohol (1.0 eq), e.g. 2-methyloxyethanol. The resulting mixture was then stirred for 30 minutes. A slurry of 5-fluoro-2-nitrophenylamine in NMP was then added slowly. The mixture was then heated to 100°C. After 2 hours, the reaction mixture was cooled and water was added. The mixture was then filtered and the captured solid was washed with water and purified by silica gel chromatography (1:1 ethyl acetate:hexane). LC/MS m/z 213.2 (MH+), R·2.24 minutes. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS m/z 183.1 (MH+), R·0.984 minutes.

Method 5

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$$NH_2$$
 NO_2 NH_2 NH_2 NH_2

Diisopropyl azodicarboxylate (1.1 eq) was added dropwise to a stirred solution of 4-amino-3-nitrophenol (1.0 eq), triphenylphosphine (1.1 eq), and an alcohol, e.g. N-(2-hydroxyethyl)morpholine (1.0 eq), in tetrahydrofuran at 0°C. The mixture was allowed to warm to room temperature and stirred for 18 hours. The solvent was evaporated, and the product was purified by silica gel chromatography (98:2 CH₂Cl₂:methanol) to yield 4-(2-morpholin-4-ylethoxy)-2-nitrophenylamine as a dark reddish-brown oil. LC/MS m/z 268.0 (MH+), R₁ 1.01 minutes. The nitroamine was reduced as in Method 1 to give the crude product which was used without further purification. LC/MS m/z 238.3 (MH+), R₁ 0.295 minutes.

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Method 6

To a flask charged with 4-amino-3-nitrophenol (1 eq), K₂CO₃ (2 eq), and 2-butanone was added an alkyl dibromide, e.g. 1,3-dibromopropane (1.5 eq). The resulting mixture was then heated at 80°C for 18 hours. After cooling, the mixture was filtered, concentrated, and diluted with water. The solution was then extracted with CH₂Cl₂ (3 x) and the combined organic layers were concentrated to give a solid that was then washed with pentane. LCMS m/z 275.1 (MH+), R₂2.74 minutes.

An acetonitrile solution of the bromide prepared above, an amine, e.g. pyrrolidine (5 eq), Cs₂CO₃ (2 eq) and Bu₄NI (0.1 eq) was heated at 70°C for 48 hours. The reaction mixture was cooled, filtered, and concentrated. The residue was dissolved in CH₂Cl₂, washed with water, and concentrated to give the desired nitroamine, 2-nitro-4-(3-pyrrolidin-1-ylpropoxy)phenylamine. LCMS m/z 266.2 (MH+), R₂1.51 minutes. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification.

Method 7

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To a suspension of 6-chloro-3-nitropyridin-2-amine (1 eq) in acetonitrile was added an amine, e.g. morpholine (4 eq). The resulting reaction mixture was stirred at 70°C for 5 hours. The solvent was evaporated under reduced pressure, and the residue triturated with ether to provide the desired compound as a bright yellow powder. LC/MS m/z 225.0 (MH+), R₁1.79 minutes.

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The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification.

Method 8:

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$$Ar$$
 OH + CI NO_2 DMF K_2CO_3 Ar O NH_2

A phenol (1 equivalent) and 5-chloro-2-nitro aniline (1 equivalent) were dissolved in DMF, and solid K₂CO₃ (2 equivalents) was added in one portion. The reaction mixture was heated at 120°C overnight. The reaction mixture was cooled to room temperature, most of the DMF was distilled off, and water was added to the residue to obtain a precipitate. The solid was dried and purified by chromatography on silicagel (2-10% MeOH/CH₂Cl₂) to afford the desired product. The nitroamine was reduced as in method 1 to give the crude product that was used without further purification.

Method 9

Furthermore, the introduction of substituents on the benzimidazole ring need not be limited to the early stages of the synthesis and may arise after formation of the quinolinone ring. For example, the crude methyl ester shown in the figure above was dissolved in a 1:1 mixture of EtOH and 30% aqueous KOH and stirred overnight at 70°C. The reaction mixture was then cooled and acidified with 1N HCl to give a precipitate. The solid was filtered, washed with water and dried to obtain 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylic acid 2-(4-amino-2-oxo-3-hydroquinolyl)benzimidazole-6-carboxylic acid as a brown solid. LC/MS m/z: 321.1 (MH+), R 2.26 minutes.

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A mixture of 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1*H*-benzimidazole-6-carboxylic acid (1 eq) the amine (1 eq), EDC (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1.2 eq), HOAT (1-hydroxy-7-azabenzotriazole, 1.2 eq) and triethylamine (2.5 eq) in DMF, was stirred at 23 °C for 20 h. The reaction mixture was partitioned between water and ethyl acetate. The combined organic layers were dried (Na₂SO₄) and concentrated. Water was added and the precipitate thus formed was filtered off and dried to afford the desired product.

The various 2-amino benzoic acid starting materials used to synthesize isatoic anhydrides may be obtained from commercial sources, prepared by methods know to one of skill in the art, or prepared by the following general Methods 10-11. General isatoic anhydride synthesis methods are described in *J. Med. Chem.* 1981, 24 (6), 735 and *J. Heterocycl. Chem.* 1975, 12(3), 565.

Method 10

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Compounds 1-3 were made using similar procedures as found in U.S. Patent No. 4,287,341. Compound 3 was reduced using standard hydrogenation conditions of 10% Pd/C in NH₄OH at 50°C over 48 hours. The product was precipitated by neutralizing with glacial acetic acid, filtering, and washing with water and ether. Yields were about 50%. Compound 5 was prepared in a manner similar to that disclosed in U.S. Patent No. 5,716,993.

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Method 11

Iodination of aniline containing compounds: Iodination was done by

a similar procedure as in J. Med. Chem. 2001, 44, 6, 917-922. The anthranilic
ester in EtOH was added to a mixture of silver sulfate (1 equivalent) and I₂ (1
equivalent). The reaction was typically done after 3 hours at room temperature.
The reaction was filtered through celite and concentrated. The residue was taken up
in EtOAc and washed with aqueous saturated NaHCO₃ (3x), water (3x), brine (1x),
dried (MgSO₄), filtered, and concentrated. The crude product (~5 g) was
dissolved in MeOH (60-100 ml), NaOH 6N (25 ml), and water (250 ml). The
reactions were typically done after heating at 70-80°C for 4 hours. The reaction
mixture was extracted with EtOAc (2x), neutralized with aqueous HCl, filtered to
collect the solids, and the solid products were washed with water. The products
were dried in vacuo.

In various instances, substitutions on the quinolinone ring may also be introduced after coupling as shown in the general methods 12-15.

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Method 12

Conversion of the C-6 or C-7 halides to an acid group was accomplished using procedures in the following references - Koga, H.; et al., *Tet.*5 *Let.*, 1995, 36, 1, 87-90 and Fukuyama, T.; et al., *J. Am. Chem. Soc.*, 1994, 116, 3125-3126.

Method 13

Conversion of the C-6 or C-7 halides to a cyano group was accomplished using procedures in the following reference - Anderson, B.A.; et al., J. Org. Chem., 1998, 63, 8224-828.

Method 14

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X = I, Br, TfO

$$\begin{array}{c}
 \text{NHR N} \\
 \text{Pd(dppf)Cl}_2/\text{Cl}_2\text{CH}_2 \\
 \text{Z} \\
 \text{Y} = B(OH)_2 \text{ or } Sn(nBu)_3
\end{array}$$

Conversion of the C-6 or C-7 halides to an aryl group was accomplished using standard Suzuki or Stille procedures such as described below.

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Suzuki Method: To a 1 dram (4 ml) vial was added sequentially the quinolone (1 equivalent), boronic acid (1.2-1.5 equivalents), Pd(dppf)Cl₂, Cl₂CH₂ (0.2 equivalents), DMF (0.5 - 1 ml) and TEA (4 equivalents). The reaction was flushed with argon, capped and heated at 85°C for 12 hours. Once done, the reaction is cooled to room temperature, and filtered with a syringe filter disk. The clear solution is then neutralized with TFA (a couple of drops) and injected directly onto a preparative HPLC. The products are lyophilized to dryness.

Stille Method: To a 1 dram (4 ml) vial was added sequentially the quinolone (1 equivalent), tin reagent (1.8 equivalent), Pd(dppf)Cl₂. Cl₂CH₂ (0.2 equivalents), and DMF (0.5 - 1 ml). The reaction was flushed with argon, capped and heated at 60-85°C for 4 hours. Once done, the reaction is cooled to room temperature, and filtered with a syringe filter disk. The clear solution is then neutralized with TFA (a couple of drops) and injected directly onto a preparative HPLC. The products are lyophilized to dryness.

15 Method 15

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A dihaloquinolone such as a difluoroquinolone (12-15 mg) was placed in a 1 dram (2 ml) vial. NMP (dry and pre-purged with argon for 5 minutes) was added to the vial (0.5 ml). The amine reagent (40-50 mg) was added next. If the amine was an HCl salt, the reaction was neutralized with TEA (~1.2-1.5 equivalents). The reaction was purged again with argon for about 5 seconds, and immediately capped. The reaction was typically heated in a heating block at 90-95°C for 18 hours. The reaction was followed by HPLC or LCMS. After taking samples for HPLC, the vial was purged with argon again and capped. Some coupling partners took 24 or 48 hours to reach completion. Less nucleophilic

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amines like pyrrole required the addition of a strong base to reach completion. In these cases, cesium carbonate (2 equivalents based on the amine used) was added to the reaction. Once done, the reaction was cooled to room temperature, and filtered with a syringe filter disk. The clear solution was then neutralized with TFA (a couple of drops) and injected directly onto a preparative HPLC. The products were lyophilized to dryness.

Example 1

Ethyl 2-benzimidazol-2-ylacetate

A solution of 1,2-phenylenediamine (1.0 eq) and ethyl 3-ethoxy-3iminopropanoate hydrochloride (1.3 eq) in ethanol was stirred at 90°C overnight.

The reaction was cooled to room temperature and the solvent was removed in vacuo. Water and CH₂Cl₂ were added to the residue. The organic layer was separated, dried over Na₂SO₄ and the solvent removed. The solid recovered was used without purification. LC/MS m/z 205.2 (MH+), R₂1.44 minutes.

15 5-(4-Methylpiperazinyl)-2-nitrobenzenecarbonitrile

5-Fluoro-2-nitrobenzenecarbonitrile (1.02 eq) and N-methylpiperazine (1.0 eq) were dissolved in NMP. Triethylamine (2.1 eq) was added, and the resulting solution heated at 100°C for 1 hour. The solution was cooled to room temperature and poured into H₂O. A precipitate formed which was filtered to yield the desired product as a green solid. LC/MS m/z 247.3 (MH+), R₂ 1.46 minutes.

2-Amino-5-(4-methylpiperazinyl)benzenecarbonitrile

5-(4-Methylpiperazinyl)-2-nitrobenzenecarbonitrile (1.0 eq) was dissolved in EtOAc. The flask was purged with nitrogen, and 10% Pd/C (0.1 eq) was added. The flask was evacuated and purged with H₂ three times. The resulting mixture was stirred for three days at room temperature. The mixture was filtered through Celite and the filter pad was washed with EtOAc. The solvent was removed *in vacuo* to give a yellow solid which was purified by silica gel

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chromatography (5:1:95 MeOH:Et₃N:EtOAc) to give the desired product as a yellow solid. LC/MS m/z 217.3 (MH+), R₂0.95 minutes.

Method A

4-Amino-3-benzimidazol-2-yl-6-(4-methylpiperazinyl)hydroquinolin-2-one

Ethyl 2-benzimidazol-2-ylacetate (1.1 eq) and 2-amino-5-(4-methylpiperazinyl)benzenecarbonitrile (1.0 eq) were dissolved in 1,2-dichloroethane, and then SnCl₄ (11 eq) was added. The mixture was heated at reflux overnight. Upon cooling, the mixture was concentrated *in vacuo*. NaOH (3 M) was added to the solid, and the mixture heated at 80°C for 0.5 hours. The solid was filtered and washed sequentially with H₂O, CH₂Cl₂, and acetone. LC/MS indicated that the product was present in the acetone layer and the solid. These fractions were combined and purified by silica gel chromatography (5-10% MeOH in CH₂Cl₂ with 1% Et₃N) to give the desired product. LC/MS *m/z* 375.4 (MH+), R₂ 1.65 minutes.

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Example 2

6-Amino-2-(2-morpholin-4-ylethoxy)benzenecarbonitrile

4-(Hydroxyethyl)morpholine (1.02 eq) was added to NaH (1.2 eq) in NMP. After 10 minutes, 6-amino-2-fluorobenzenecarbonitrile (1.0 eq) was added in NMP. The resulting mixture was heated at 100°C for 1 hour. The mixture was then cooled and poured into H₂O. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to a yield a brown gum. The crude material was purified by silica gel chromatography (5:1:95 MeOH:Et₃N:EtOAc) to give the desired product. LC/MS m/z 248.3 (MH+), R₂1.26 minutes.

4-Amino-3-benzimidazol-2-yl-5-(2-morpholin-4-ylethoxy)hydroquinolin-2-oneThe title compound was synthesized as described in Example 1, Method A using 6-amino-2-(2-morpholin-4-ylethoxy)benzenecarbonitrile. LC/MS m/z 406.4 (MH+), R 1.67 minutes.

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Example 3

4-(2-Morpholin-4-ylethoxy)-2-nitrophenylamine

Diisopropyl azodicarboxylate (1.1 eq) was added dropwise to a stirred solution of 4-amino-3-nitrophenol (1.0 eq), triphenylphosphine (1.1 eq), and N-(2-hydroxyethyl)morpholine (1.0 eq), in THF at 0°C. The mixture was allowed to warm to room temperature and left to stir for 18 hours. The solvent was evaporated and the product was purified by silica gel chromatography (98:2 CH₂Cl₂:MeOH) to yield a dark reddish-brown oil. LC/MS *m/z* 268.0 (MH+), R₂ 1.01 minutes.

10 4-(2-Morpholin-4-ylethoxy)benzene-1,2-diamine

To a solution 4-(2-morpholin-4-ylethoxy)-2-nitrophenylamine (1.0 eq) in EtOH was added Pd/C (0.1 eq). The reaction vessel was repeatedly purged with nitrogen, then stirred under a hydrogen atmosphere (1 atm) for 18 hours. The product was filtered through a Celite plug, and the plug washed with EtOH. The diamine was used without purification. LC/MS m/z 238.3 (MH+), R_r 0.295 minutes.

Ethyl 2-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]acetate

The title compound was synthesized as described in Example 1 using 4-(2-morpholin-4-ylethoxy)benzene-1,2-diamine. The organic layer was concentrated and the residue was purified by silica gel chromatography (10:1:2 CH₂Ch:MeOH:EtOAc) to yield a dark reddish brown oil. LC/MS m/z 334.4 (MH+) R₂ 1.08 minutes.

$\hbox{$4$-Amino-3-[5-(2-morpholin-4-ylethoxy)$benzimidazol-2-yl]-$6$-nitrohydroquinolin-2-one}$

The title compound was synthesized as described in Example 1, Method A using ethyl 2-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]acetate and 5-nitroanthranilonitrile. The crude product was purified by silica gel chromatography (5-10% MeOH in CH₂Cl₂ with 1% Et₃N) to give the desired product. LC/MS m/z 451.2 (MH+), R₂1.89 minutes.

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Example 4

4-Amino-5-(2-morpholin-4-ylethoxy)-3-[5-(2-morpholin-4-ylethoxy)-benzimidazol-2-yl]hydroquinolin-2-one

The title compound was synthesized as described in Example 1,

Method A using ethyl 2-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]acetate and
6-amino-2-(2-morpholin-4-ylethoxy)benzenecarbonitrile. LC/MS m/z 535.4

(MH+), R 1.44 minutes.

Example 5

2-[(Ethoxycarbonyl)methyl]benzimidazole-5-carboxylic acid

The title compound was synthesized as described in Example 1 using 3,4-diaminobenzoic acid. The crude material was purified by silica gel chromatography (5:95 MeOH:CH₂Cl₂) to afford the desired product as a white to off-white solid. LC/MS m/z 249.1 (MH+), R₁ 1.35 minutes.

Ethyl 2-[5-(N,N-dimethylcarbamoyl)benzimidazol-2-yl]acetate

2-[(Ethoxycarbonyl)methyl]benzimidazole-5-carboxylic acid (1.0 eq) was dissolved in THF. HBTU (1.1 eq) and diisopropylethylamine (2.0 eq) were added, followed by dimethylamine (2.0 M in THF, 1.1 eq). The reaction was stirred at room temperature overnight then concentrated and the resulting residue was purified by silica gel chromatography (5:95 MeOH:CH₂Cl₂) to afford the desired compound. LC/MS m/z 276.2 (MH+), R₁1.18 minutes.

[2-(4-amino-2-oxo(3-hydroquinolyl))benzimidazol-5-yl]-N,N-dimethylcarboxamide.

The title compound was synthesized as described in Example 1, Method A using ethyl 2-[5-(N,N-dimethylcarbamoyl)benzimidazol-2-yl]acetate and anthranilonitrile. The resulting solid was collected by filtration and washed with water followed by acetone to afford the desired product as a white solid. LC/MS m/z 348.3 (MH+), R 1.87 minutes.

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Example 6

$\hbox{\it 4-}Amino-\hbox{\it 3-[5-(morpholin-4-ylcarbonyl)} benzimidazol-\hbox{\it 2-yl]} hydroquinolin-\hbox{\it 2-one.}$

2-[(Ethoxycarbonyl)methyl]benzimidazole-5-carboxylic acid (1.0 eq) was dissolved in THF. HBTU (1.1 eq) and diisopropylethylamine (2.0 eq) were added, followed by morpholine (1.1 eq). The reaction was stirred at room temperature for 3 days then concentrated and purified by silica gel chromatography (5-10% methanol/dichloromethane). The product-containing fractions were concentrated and dissolved in anhydrous 1,2-dichloroethane. Anthranilonitrile (1.0 eq) was added followed by SnCl4 (5.0 eq) and the reaction was heated at 90°C overnight. The reaction mixture was concentrated and the resulting residue was redissolved in NaOH (2 M) and heated at 90°C for 4 hours. After cooling to room temperature, the resulting solid was collected and washed with water followed by acetone to afford the desired product. LC/MS m/z 390.2 (MH+), R 1.95 minutes.

Example 7

15 4-Bromobenzene-1,2-diamine

A solution of 4-bromo-2-nitroaniline (1.0 eq) and $SnCl_2(2.2 eq)$ in EtOH was heated at reflux for 3 hours. After this time, the solution was poured onto ice, brought to pH 10 with 2M NaOH and extracted with Et2O. The combined organic layers were dried over MgSO4 and concentrated. The resulting brown oil was purified by silica gel chromatography (0-50% EtOAc:hexanes) to provide a light yellow solid. LC/MS m/z 187.1 (MH+), R_t 1.33 minutes.

2-Nitro-4-(2-thienyl)phenylamine

4-Bromo-2-nitroaniline (1.0 eq) and Na₂CO₃ (2.0 eq) were dissolved in DMF/H₂O (5:1) at room temperature. Nitrogen was bubbled through the reaction mixture for 5 minutes and PdCl₂(dppf)₂ (0.1 eq) was added. After stirring at 23°C for approximately 10 minutes, 2-thiopeneboronic acid (1.1 eq) in DMF was added and the reaction was heated at 90°C for 12 hours. After this time, the solution was concentrated and partitioned between EtOAc and H₂O. The layers were separated and the aqueous layer was extracted with EtOAc. The combined

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organic layers were dried over MgSO₄ and concentrated under reduced pressure. The resulting black residue was purified by silica gel chromatography (0-20% EtOAc:hexanes) to yield an orange solid. LC/MS m/z 221.1 (MH+), R₁2.67 minutes.

5 Ethyl 2-[5-(2-thienyl)benzimidazol-2-yl]acetate

2-Nitro-4-(2-thienyl)phenylamine (1.0 eq) and 10% Pd/C (0.1 eq) were suspended in anhydrous EtOH at room temperature. The reaction flask was evacuated and subsequently filled with H₂. The resulting mixture was allowed to stir under a hydrogen atmosphere for 3 hours. Ethyl 3-ethoxy-3-iminopropanoate hydrochloride (2.0 eq) was then added and the resulting mixture was heated at reflux for 12 hours. After this time, the solution was filtered through a plug of Celite, concentrated, dissolved in 50 ml of 2N HCl and washed with CH₂Cl₂. The aqueous layer was brought to pH 12 with concentrated NH₄OH(aq) and extracted with CH₂Cl₂. The combined organic layers were dried with MgSO₄ and concentrated to yield a brown oil which was purified by silica gel chromatography (5:95 MeOH:CH₂Cl₂) to provide a yellow solid. LC/MS *m/z* 287.1 (MH+), R₄ 1.98 minutes.

4-Amino-3-[5-(2-thienyl)benzimidazol-2-yl]hydroquinolin-2-one

The title compound was synthesized as described in Example 1,

Method A using ethyl 2-[5-(2-thienyl)benzimidazol-2-yl]acetate and
anthranilonitrile. LC/MS m/z 359.2 (MH+), Rr 2.68 minutes.

Example 8

5-Fluoro-2-nitrophenylamine

2,4-Difluoronitrobenzene (1.0 eq) was placed in a dry roundbottomed flask equipped with a dry ice condenser charged with acetone/dry ice.
Ammonia was condensed into the flask and the resulting solution was stirred at reflux for 7 hours. A yellow precipitate was formed within 1 hours. After 7 hours, the condenser was removed and the liquid ammonia was allowed to evaporate over several hours. The crude product was purified by flash chromatography on silica

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gel (85:15 hexanes:EtOAc, product at $R_f = 0.32$, contaminant at $R_f = 0.51$). GC/MS m/z 156.1 (M+), R_f 11.16 minutes.

2-Nitro-5-[1-(1,2,4-triazolyl)]phenylamine

5-Fluoro-2-nitrophenylamine (1.0 eq), 1H-1,2,4-triazole (3.0 eq) and NaH (3.0 eq) in NMP were heated at 100°C for 1 hour. The solution was cooled to room temperature and slowly poured onto ice water. The resulting precipitate was filtered and dried under vacuum to yield the desired product. The resulting solid was recrystallized from EtOH to afford pure product as a bright yellow solid. LC/MS m/z 206.2 (MH+), R 1.88 minutes.

10 Ethyl 2-{5-[1-(1,2,4-triazolyl)]benzimidazol-2-yl}acetate

The title compound was synthesized as described in Example 7 using 2-nitro-5-[1-(1,2,4-triazolyl)] phenylamine. LC/MS m/z 272.1 (MH+), R₁ 1.19 minutes.

$\textbf{4-Amino-3-} \textbf{\{5-[1-(1,2,4-triazolyl)]} benzimidazol-2-yl\} hydroquinolin-2-one$

The title compound was synthesized as described in Example 1, Method A using ethyl 2-{5-[1-(1,2,4-triazolyl)]benzimidazol-2-yl}acetate and anthranilonitrile. The crude solid was collected and purified by silica gel chromatography (92:7:1 CH₂Cl₂:MeOH:Et₃N). LC/MS m/z 344.3 (MH+), R₂ 2.01 minutes.

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Example 9

Method B

N-(4-Chloro-2-cyanophenyl)-2-(5-morpholin-4-ylbenzimidazol-2-yl)acetamideLiHMDS (2.5 eq) was added to ethyl 2-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]acetate (1.0 eq) in THF at -78°C. After 1 hour, 2-amino-5-chlorobenzenecarbonitrile (0.82 eq) in THF was added. The reaction was allowed to warm to 23°C and stirred overnight. The resulting mixture was quenched with NH4Cl (aqueous saturated solution) and extracted with EtOAc. The combined organic layers were washed with H2O and brine, dried over Na2SO4,

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filtered and concentrated *in vacuo* to yield a brown solid. The crude material was purified by silica gel chromatography (5:1 EtOAc:hexane) to give the desired product. LC/MS m/z 396.1 (MH+), R 1.79 minutes.

4-Amino-6-chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

N-(4-chloro-2-cyanophenyl)-2-(5-morpholin-4-ylbenzimidazol-2-yl)acetamide (1.0 eq) was heated in NaOMe (0.5 M in MeOH, 18 eq) at 70°C for 2 hours. The resulting mixture was cooled, and the resulting solid was filtered and washed with water to give the desired product. LC/MS m/z 396.4 (MH+), R₁2.13 minutes.

10 <u>Example 10</u>

2-Nitro-5-piperidylphenylamine

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The title compound was synthesized as described in Example 8 using piperidine (3.0 eq, excess acts as base in place of NaH). The desired product was obtained as a yellow, crystalline solid. LC/MS m/z 222.2 (MH+), R₂ 2.53 minutes.

Ethyl 2-(5-piperidylbenzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 7 using 2-nitro-5-piperidylphenylamine. The desired product was obtained as a yellow oil. LC/MS m/z 288.3 (MH+), R_i 1.31 minutes.

20 4-amino-3-(5-piperidylbenzimidazol-2-yl)hydroquinolin-2-one

The title compound was synthesized as described in Example 9, Method B using ethyl 2-(5-piperidylbenzimidazol-2-yl)acetate and anthranilonitrile. The acyclic amide was used crude in the NaOMe cyclization step. The desired product was obtained following purification by silica gel chromatography (96.5:3.0:0.5 CH₂Cl₂:MeOH:Et₃N, R_f 0.2). LC/MS m/z 360.4 (MH+), R_f 1.83 minutes.

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Example 11

[1-(3-Amino-4-nitrophenyl)pyrrolidin-3-yl]dimethylamine

The title compound was synthesized as described in Example 8 using 3-(dimethylamino)pyrrolidine (3.0 eq, excess amine was used as the base in place of NaH). LC/MS m/z 251.3 (MH+), R₁ 1.25 minutes.

Ethyl 2-{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl}acetate

The title compound was synthesized as described in Example 7 using [1-(3-amino-4-nitrophenyl)pyrrolidin-3-yl]dimethylamine. The desired product was obtained as a yellow oil. LC/MS m/z 317.4 (MH+), R 1.36 minutes.

10 2-{5-[3-(Dimethylamino)pyrrolidinyl]benzimidazol-2-yl}-*N*-(4-chloro-2-cyanophenyl)acetamide

The title compound was synthesized as described in Example 9, Method B using ethyl 2-{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl}acetate. LC/MS m/z 423.4 (MH+), R 1.67 minutes.

4-Amino-3-{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl}-6-chlorohydroquinolin-2-one

The title compound was synthesized as described in Example 9, Method B using 2- $\{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl\}-N-(4-chloro-2-cyanophenyl)acetamide. LC/MS <math>m/z$ 423.4 (MH+), R 1.71 minutes.

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Example 12

Ethyl 2-[5-(dimethylamino)benzimidazol-2-yl]acetate

The title compound was synthesized as described in Example 7 using (3-amino-4-nitrophenyl)dimethylamine. The resulting tan film was purified by silica gel chromatography (5:1:94 MeOH:EtaN:CH2Cl2) to give the desired product.

25 LC/MS 248.3 m/z (MH+), R₁.24 minutes.

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2-[5-(Dimethylamino)benzimidazol-2-yl]-N-(2-cyanophenyl)acetamide

The title compound was synthesized as described in Example 9, Method B using ethyl 2-[5-(dimethylamino)benzimidazol-2-yl]acetate and anthranilonitrile. LC/MS m/z 320.2 (MH+), R 1.68 minutes.

5 4-Amino-3-[5-(dimethylamino)benzimidazol-2-yl]hydroquinolin-2-one

The title compound was synthesized as described in Example 9,

Method B using 2-[5-(dimethylamino)benzimidazol-2-yl]-N-(2-

cyanophenyl)acetamide. LC/MS m/z 320.2 (MH+), R 1.72 minutes.

Example 13

10 Ethyl 2-(5-cyanobenzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 7 using 4-amino-3-nitro-benzonitrile. LC/MS m/z 230.2 (MH+), R₁ 1.29 minutes.

2-(4-Amino-2-oxo-3-hydroquinolyl)benzimidazole-5-carbonitrile

The title compound was synthesized as described in Example 9,

Method B using ethyl 2-(5-cyanobenzimidazol-2-yl)acetate and anthranilonitrile (no acyclic amide observed so the NaOMe step was not needed). LC/MS m/z 302.3

(MH+), R₂ 2.62 minutes.

Example 14

2-(4-Amino-2-oxo-3-hydroquinolyl)benzimidazole-5-carboxamidine

- 2-(4-Amino-2-oxo-3-hydroquinolyl)benzimidazole-5-carbonitrile (1.0 eq) in EtOH was placed into a glass bomb, cooled to 0°C and HCl (g) was bubbled through for 15 minutes. The bomb was then sealed, brought to room temperature and stirred overnight. The solvent was removed in vacuo. The residue was dissolved in EtOH in a glass bomb and cooled to 0°C. NH₃(g) was bubbled
- 25 through for 15 minutes and the bomb was sealed and heated to 80°C for 5 hours.

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The solvent was removed in vacuo and the crude product was purified by reversed-phase HPLC. LC/MS m/z 319.2 (MH+), R 1.70 minutes.

Example 15

4-Amino-3-[5-(2-morpholin-4-ylethoxy)-benzimidazol-2-yl]hydroquinolin-2-one

The title compound was synthesized as described in Example 9, Method B using anthranilonitrile. The crude acyclic amide was used without purification in the NaOMe cyclization step. The crude final product was purified by reversed-phase HPLC (DMSO/5% TFA). LC/MS m/z 406.4 (MH+), R 1.56 minutes.

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Example 16

5-Morpholin-4-yl-2-nitrophenylamine

The title compound was synthesized as described in Example 8 using morpholine (3.0 eq, excess amine was used as the base in place of NaH). LC/MS m/z 224.1 (MH+), R 1.89 minutes.

15 Ethyl 2-(5-morpholin-4-ylbenzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 7 using 5-morpholin-4-yl-2-nitrophenylamine. The crude yellow oil was purified by silica gel chromatography (89.5:10:0.5 CH₂Cl₂:MeOH:Et₃N) to yield the desired product as a yellow solid. LC/MS m/z 290.3 (MH+), R₂ 1.31 minutes.

20 Method C

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$\hbox{\it 4-Hydroxy-3-(5-morpholin-4-ylbenzimid} azol-\hbox{\it 2-yl)-1-benzylhydroquin} olin-\hbox{\it 2-one}$

To a solution of ethyl 2-(5-morpholin-4-ylbenzimidazol-2-yl)acetate (1.0 eq) in anhydrous THF at -78°C under an atmosphere of nitrogen was added LiHMDS (1 M in THF, 3.1 eq) and the solution was stirred for 1 hour. A solution of 1-benzylbenzo[d]1,3-oxazaperhydroine-2,4-dione (1.05 eq) in anhydrous THF was then added dropwise and the resulting solution was allowed to warm to 0°C

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over 1 hour. The resulting mixture was quenched with a saturated aqueous solution of ammonium chloride and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (4 times). The combined organic layers were dried over Na₂SO₄, concentrated *in vacuo*, and the crude material was dissolved in toluene and heated at reflux for 16 hours. The toluene was removed *in vacuo* and the crude material was used without further purification. The product was obtained as a white solid. LC/MS m/z 453.1 (MH+), R 2.91 minutes.

4-Hydroxy-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

Crude 4-hydroxy-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-

benzylhydroquinolin-2-one (1.0 eq) was dissolved in trifluoromethanesulfonic acid and heated at 40°C for 16 hours. The resulting solution was diluted with water and neutralized with 6 N NaOH (aq), whereupon a yellow precipitate formed. The crude solid was isolated by centrifugation and purified by reversed-phase HPLC to produce the desired product as a bright yellow solid. LC/MS m/z 363.3 (MH+), R. 1.77 minutes.

Example 17

N-[1-(3-Amino-4-nitrophenyl)pyrrolidin-3-yl](tert-butoxy)carboxamide

The title compound was synthesized as described in Example 8 using 3-(tert-butoxycarbonylamino)pyrrolidine (1.01 eq) with disopropylethylamine (2.0 eq) as the base (in place of NaH). The product was obtained as an orange, crystalline solid. LC/MS m/z 323.3 (MH+), R_z 2.53 minutes.

Ethyl 2-(5-{3-[(tert-butoxy)carbonylamino]pyrrolidinyl}benzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 7 using

N-[1-(3-amino-4-nitrophenyl)pyrrolidin-3-yl](tert-butoxy)carboxamide. The product was obtained as a yellow oil. LC/MS m/z 323.3 (MH+), R 2.53 minutes.

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3-[5-(3-aminopyrrolidinyl)benzimidazol-2-yl]-4-hydroxyhydroquinolin-2-one

The title compound was synthesized following the procedure described in Example 16, Method C using ethyl 2-(5-{3-[(tert-butoxy)carbonylamino]pyrrolidinyl}benzimidazol-2-yl)acetate. The product was obtained as a yellow solid following cleavage of the benzyl group (see procedure in Example 15). LC/MS *m/e* 362.3 (MH+), R_t 1.55 minutes.

Example 18

(3-Amino-4-nitrophenyl)[2-(dimethylamino)ethyl]methylamine

The title compound was synthesized as described in Example 8 using 1,1,4-trimethylethylenediamine (1.01 eq) with disopropylethylamine (2.0 eq) as the base (in place of NaH). The product was obtained as a bright yellow, crystalline solid. LC/MS m/z 239.3 (MH+), R₁ 1.29 minutes.

Ethyl 2-(5-{[2-(dimethylamino)ethyl]methylamino}benzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 7 using (3-amino-4-nitrophenyl)[2-(dimethylamino)ethyl]methylamine. The desired product was obtained as a yellow oil. LC/MS m/z 305.2 (MH+), R 1.17 minutes.

$3-(5-\{[2-(Dimethylamino)ethyl]methylamino\}\ benzimidazol-2-yl)-4-hydroxy-1-benzylhydroquinolin-2-one$

The title compound was synthesized as described in Example 16,

Method C using ethyl 2-(5-{[2-(dimethylamino)ethyl]methylamino}benzimidazol-2yl)acetate. The product was obtained as a pale yellow solid. LC/MS m/z 468.4
(MH+), R 2.26 minutes.

3-(5-{[2-(Dimethylamino)ethyl]methylamino}benzimidazol-2-yl)-4-hydroxyhydroquinolin-2-one

The title compound was synthesized as described in Example 16,

Method C using 3-(5-{[2-(dimethylamino)ethyl]methylamino}benzimidazol-2-yl)-4hydroxy-1-benzylhydroquinolin-2-one. The crude material was purified by

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reversed-phase HPLC to yield the product as a yellow solid. LC/MS m/z 378.4 (MH+), R 1.99 minutes.

Example 19

Method D

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5 4-Chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one

A solution of 4-hydroxy-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one (1.0 eq) and POCl₃ in a dry, round-bottomed flask was heated at 80°C for 2 hours. The excess POCl₃ was removed *in vacuo* and the crude material was quenched with water. The crude product was collected by filtration and purified by silica gel chromatography (1:9 MeOH:CH₂Cl₂). 4-Chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one was isolated as a red solid. LC/MS *m/z* 471.4 (MH+), R₂ 2.35 minutes.

$\hbox{$4$-[(2-Methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one } \\$

A solution of 4-chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one (1.0 eq) and EtOH was treated with 2-methoxyethylamine (10 eq) at room temperature. The resulting solution was heated at reflux for 16 hours and then the solvent was removed *in vacuo*. The crude solid was sonicated in water, filtered, sonicated in hexanes, and filtered again. The crude product was used without further purification. LC/MS *m/z* 510.4 (MH+), R₁ 2.20 minutes.

4-[(2-Methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

4-[(2-methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-125 benzylhydroquinolin-2-one was debenzylated using the procedure described in
Example 16 to produce the title compound. LC/MS m/z 420.2 (MH+), R_t 1.57
minutes. 4-[(2-hydroxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2yl)hydroquinolin-2-one was produced as a side product (see below).

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4-[(2-hydroxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

The title compound was obtained as a side-product of the debenzylation of 4-[(2-methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16 and was isolated by reversed-phase HPLC as a yellow solid. LC/MS m/z 406.2 (MH+), R_t 1.39 minutes.

Example 20

4-(Methoxyamino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19, Method D using O-methylhydroxylamine. The product was used without purification.

4-(Methoxyamino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

The title compound was obtained as a yellow solid after debenzylation of 4-(methoxyamino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS m/z 392.2 (MH+), R 1.82 minutes.

Example 21

20 *tert*-Butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}piperidinecarboxylate

The title compound was synthesized as described in Example 19, Method D using 1-tert-butoxycarbonyl-3-aminopiperidine. The product was used without purification.

25 3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-(3-piperidylamino)hydroquinolin-2-one

The product was obtained as a yellow solid after debenzylation of tert-butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}piperidinecarboxylate using the procedure described in

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Example 16. The t-butoxycarbonyl group is removed under the reaction conditions. LC/MS m/z 445.4 (MH+), R_i 1.73 minutes.

Example 22

tert-Butyl-3-({[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}methyl)piperidinecarboxylate

The title compound was synthesized as described in Example 19, Method D using 1-tert-butoxycarbonyl-3-aminomethylpiperidine. The product was used without purification.

3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-[(3-piperidylmethyl)amino]-10 hydroquinolin-2-one

The title compound was obtained as a yellow solid after debenzylation of *tert*-butyl-3-({[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}methyl)piperidinecarboxylate using the procedure described in Example 16. LC/MS *m/z* 459.6 (MH+), R₁ 1.71 minutes.

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Example 23

 $\hbox{\it 4-{[2-(Dimethylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one}$

The title compound was synthesized as described in Example 19, Method D using 1,1-dimethylethylenediamine. The product was used without purification.

 $\label{lem:conditional} $$4-\{[2-(Dimethylamino)+3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one$

The title compound was obtained as a yellow solid after debenzylation of 4-{[2-(dimethylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS m/z 433.4 (MH+), R₂ 1.55 minutes.

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Example 24

 ${\it 3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-[(oxolan-2-ylmethyl)amino]-1-benzylhydroquinolin-2-one}$

The title compound was synthesized as described in Example 19,

Method D using 2-aminomethyltetrahydrofuran. The product was used without purification.

3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-[(oxolan-2-ylmethyl)amino]-hydroquinolin-2-one

The title compound was obtained as a yellow solid after

debenzylation of 3-(5-morpholin-4-ylbenzimidazol-2-yl)-4-[(oxolan-2-ylmethyl)amino]-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS m/z 446.5 (MH+), R₂ 2.19 minutes.

Example 25

4-{[2-(Methylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19, Method D using 1-tert-butoxycarbonyl-1-methylethylenediamine. The product was used without purification.

 $\begin{array}{lll} & 4-\{[2-(Methylamino)ethyl]amino\}-3-(5-morpholin-4-ylbenzimidazol-2-\\ 20 & yl)hydroquinolin-2-one \end{array}$

The title compound was obtained as a yellow solid after debenzylation of 4-{[2-(methylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. The t-butoxycarbonyl group is removed under the reaction conditions.

25 LC/MS m/z 419.4 (MH+), R 1.50 minutes.

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Example 26

tert-Butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}pyrrolidinecarboxylate

The title compound was synthesized as described in Example 19,

Method D using 1-tert-butoxycarbonyl-3-aminopyrrolidine. The product was used without purification.

3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-(pyrrolidin-3-ylamino)hydroquinolin-2-one

The title compound was obtained as a yellow solid after

debenzylation of *tert*-butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}pyrrolidinecarboxylate using the procedure described in Example 16. LC/MS *m/z* 431.4 (MH+), R 1.50 minutes.

Example 27

4-[((2S)-2-Amino-4-methylpentyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-15 1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19, Method D using (2S)-2-tert-butoxycarbonylamino-4-methylpentylamine. The product was used without purification.

4-[((2S)-2-Amino-4-methylpentyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

The title compound was obtained as a yellow solid after debenzylation of 4-[((2S)-2-amino-4-methylpentyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS m/z 461.4 (MH+), R 1.78 minutes.

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Example 28

t-Butoxycarbonyl protected 4-[((2S)-2-amino-3-methylbutyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19,

Method D using (2S)-2-tert-butoxycarbonylamino-3-methylbutylamine. The product was used without purification.

4-[((2S)-2-Amino-3-methylbutyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

The title compound was obtained as a yellow solid after

debenzylation of 4-[((2S)-2-amino-3-methylbutyl)amino]-3-(5-morpholin-4ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in
Example 16. The t-butoxycarbonyl group is removed under the reaction conditions.

LC/MS m/z 447.5 (MH+), R₁ 2.96 minutes.

Example 29

4-Amino-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one
The title compound was synthesized as described in Example 19,
Method D using ammonia in a sealed glass tube. The product was used without purification.

4-Amino-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

The title compound was obtained as a bright yellow solid after debenzylation of 4-amino-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16 and purification by reversed-phase HPLC. LC/MS m/z 362.3 (MH+), R 1.61 minutes.

Example 30

25 3-Benzimidazol-2-yl-4-hydroxy-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 16, Method C using ethyl 2-benzimidazol-2-ylacetate. The product was obtained as a

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white solid and used without further purification. LC/MS m/z 368.4 (MH+), Rr 2.99 minutes.

3-(Benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19,

Method D using 3-benzimidazol-2-yl-4-hydroxy-1-benzylhydroquinolin-2-one. The crude product was used without purification.

Example 31

3-Benzimidazol-2-yl-4-(methylamino)hydroquinolin-2-one

The benzylated title compound was synthesized as described in

Example 19, Method D using methylamine and 3-(benzimidazol-2-yl)-4-chloro-1benzylhydroquinolin-2-one. The product was obtained after debenzylation as a
yellow solid using the procedure described in Example 16. LC/MS m/z 291.3

(MH+), R₁ 1.64 minutes.

Example 32

15 3-Benzimidazol-2-yl-4-(ethylamino)hydroquinolin-2-one

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The benzylated title compound was synthesized as described in Example 19, Method D using ethylamine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 305.3 (MH+), R₂ 2.01 minutes.

Example 33

3-Benzimidazol-2-yl-4-[(oxolan-2-ylmethyl)amino]hydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using 2-aminomethyltetrahydrofuran and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 361.2 (MH+), R 1.74 minutes.

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Example 34

3-Benzimidazol-2-yl-4-[(4-piperidylmethyl)amino]hydroquinolin-2-one

The protected title compound was synthesized as described in Example 19, Method D using 1-tert-butoxycarbonyl-4-aminomethylpiperidine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after deprotection and debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 374.3 (MH+), R₁ 1.29 minutes.

Example 35

3-Benzimidazol-2-yl-4-[(4-fluorophenyl)amino]hydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using 4-fluoroaniline and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 371.2 (MH+), R 1.92 minutes.

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Example 36

3-Benzimidazol-2-yl-4-(methoxyamino)hydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using O-methylhydroxylamine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 307.3 (MH+), R₁ 1.77 minutes.

Example 37

3-Benzimidazol-2-yl-4-(benzimidazol-6-ylamino)hydroquinolin-2-one

The benzylated title compound was synthesized as described in

Example 19, Method D using 5-aminobenzimidazole and 3-(benzimidazol-2-yl)-4chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after
debenzylation as a yellow solid using the procedure described in Example 16.

LC/MS m/z 393.4 (MH+), R 1.41 minutes.

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Example 38

3-Benzimidazol-2-yl-4-(phenylamino)hydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using aniline and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 353.4 (MH+), Rr 2.38 minutes.

Example 39

3-Benzimidazol-2-yl-4-(quinuclidin-3-ylamino)hydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using 3-aminoquinuclidine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 386.4 (MH+), R 1.82 minutes.

15 <u>Example 40</u>

3-Benzimidazol-2-yl-4-[(imidazol-5-ylmethyl)amino]hydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using 4-aminomethyl-1H-imidazole and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 357.4 (MH+), R 1.34 minutes.

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Example 41

3-Benzimidazol-2-yl-4-(morpholin-4-ylamino)hydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using 4-aminomorpholine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS m/z 362.4 (MH+), R·1.42 minutes.

Example 42

3-Benzimidazol-2-yl-4-hydrazinohydroquinolin-2-one

The benzylated title compound was synthesized as described in Example 19, Method D using hydrazine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained as a yellow solid after debenzylation using the procedure described in Example 16. LC/MS m/z 292.3 (MH+), R 1.19 minutes.

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Example 43

3-Benzimidazol-2-yl-2-oxohydroquinoline-4-carbonitrile

3-Benzimidazol-2-yl-4-chloro-1-benzylhydroquinolin-2-one (1 eq) was dissolved in DMA, and CuCN (10 eq) was added in one portion. The reaction mixture was stirred at 90°C overnight. The resulting mixture was allowed to cool to room temperature, water was added, and the orange precipitate was removed by filtration. The solid was treated with a solution of hydrated FeCl₃ at 70°C for 1 hour. The suspension was centrifuged and the solution removed. The remaining solid was washed with 6N HCl (2 times), sat. Na₂CO₃ (2 times), water (2 times) and lyophilized. The resulting powder was dissolved in 1 mL of triflic acid and heated at 60°C overnight. The resulting mixture was cooled to 0°C and water was slowly added. Saturated LiOH was added dropwise to the suspension to a pH of 8, then the solid was filtered and washed with water (3 times). Purification by reversed-phase HPLC afforded the desired product. LC/MS m/z 287.1 (MH+), Re 1.89 minutes.

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Example 44

Ethyl 2-(5,6-dimethylbenzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 1 using 4,5-dimethylbenzene-1,2-diamine. The crude yellow oil was purified first by silica gel chromatography (96.5:3.0:0.5, CH₂Cl₂:MeOH:Et₃N), and then by recrystallization from toluene to yield the title compound as a pale, yellow solid. LC/MS m/z 233.1 (MH+), R₁ 1.73 minutes.

3-(5,6-Dimethylbenzimidazol-2-yl)-4-hydroxy-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 16, Method C using ethyl 2-(5,6-dimethylbenzimidazol-2-yl)acetate. The crude material was purified by silica gel chromatography (98.5:1.5, CH₂Cl₂:MeOH) to yield the title compound as a yellow solid. LC/MS m/z 396.2 (MH+), R₁ 3.60 minutes.

3-(5,6-Dimethylbenzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19, Method D using 3-(5,6-dimethylbenzimidazol-2-yl)-4-hydroxy-1-benzylhydroquinolin-2-one. The title compound was obtained as an orange-yellow solid. LC/MS m/z 414.2 (MH+), R₁ 2.47 minutes.

tert-Butyl 3-{[3-(5,6-dimethylbenzimidazol-2-yl)-2-oxo-1-benzyl-4hydroquinolyl]amino}piperidinecarboxylate

The title compound was synthesized as described in Example 19, Method D using 1-tert-butoxycarbonyl-3-aminopiperidine. The crude material was purified by silica gel chromatography (99:1 CH₂Cl₂:MeOH) to yield the title compound as a yellow solid. LC/MS m/z 578.5 (MH+), R_t 3.05 minutes.

3-(5,6-Dimethylbenzimidazol-2-yl)-4-(3-piperidylamino)hydroquinolin-2-one

tert-Butyl 3-{[3-(5,6-dimethylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}piperidine-carboxylate was debenzylated as described in

Example 16. The crude material was purified by reversed-phase HPLC to yield the

title compound as a light yellow solid. LC/MS m/z 388.4 (MH+), R 1.61 minutes.

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Example 45

3*H*-Imidazo[4,5-*b*]pyridin-2-ylacetonitrile

Ethyl cyanoacetate (1.5 eq) and 2,3-diaminopyridine (1 eq) were heated at 185°C for 30 minutes. The reaction mixture was cooled to room temperature and the black solid was triturated with ether. The desired product was thus obtained as a dark brown powder. LC/MS m/z 159.1 (MH+), R₁0.44 minutes.

Ethyl 3*H*-imidazo[4,5-*b*]pyridin-2-ylacetate

3*H*-Imidazo[4,5-*b*]pyridin-2-ylacetonitrile was suspended in EtOH, and gaseous HCl was bubbled through for 3 hours. The suspension initially seemed to dissolve, but a precipitate started forming almost immediately. The reaction mixture was cooled to 0°C and a cold saturated NaHCO3 solution was carefully added. Solid NaHCO3 was also added to bring the pH to a value of 7.6. The aqueous phase was then extracted with EtOAc, and the organic extracts were dried (Na2SO4). After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on silicagel (10% MeOH in CH2Cl2 with 1% Et3N) providing the desired product as a light brown solid. LC/MS *m/z* 206.1 (MH+), R₂ 0.97 minutes.

20 4-Amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one

LiHMDS (3.0 eq) was added to ethyl 3*H*-imidazo[4,5-*b*]pyridin-2-ylacetate (1.0 eq) in THF at -78°C. After 20 minutes, a solution of 2-aminobenzenecarbonitrile (1.1 eq) in THF was added. The resulting mixture was allowed to warm to room temperature, stirred for 3 hours, and then refluxed overnight. The mixture was cooled to 0°C and quenched with an aqueous saturated NH₄Cl solution. A precipitate formed, was filtered off, and was washed repeatedly with ether to yield the desired compound as a light brown solid. LC/MS *m/z* 278.2 (MH+), R-1.82 minutes.

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Example 46

6-Morpholin-4-yl-3-nitropyridin-2-amine

Morpholine (4 eq) was added to a suspension of 6-chloro-3-nitropyridin-2-amine (1 eq) in CH₃CN, and the reaction mixture was stirred at 70° C for 5 hours. The solvent was evaporated under reduced pressure, and the residue was triturated with ether to afford the desired compound as a bright yellow powder. LC/MS m/z 225.0 (MH+), R₁.79 minutes.

Ethyl (5-morpholin-4-yl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)acetate

To a solution 6-chloro-3-nitropyridin-2-amine (1.0 eq) in EtOH was added Pd/C (0.1 eq). The reaction vessel was repeatedly purged with hydrogen and then stirred under a hydrogen atmosphere (1 atm) for 18 hours. Ethyl 3-ethoxy-3-iminopropanoate hydrochloride (2.0 eq) was added in one portion, and the reaction mixture was refluxed overnight. The reaction mixture was cooled to room temperature, filtered through a celite plug, and the plug was washed with EtOH.

After evaporation of the solvent under reduced pressure, the residue was purified by silica gel chromatography (5% MeOH in CH₂Cl₂ with 1% Et₃N) providing the desired product as a brown solid. LC/MS m/z 291.3 (MH+), R₁ 1.71 minutes.

4-Amino-3-(5-morpholin-4-yl-3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one

The title compound was synthesized as described in Example 45,

20 Method E using ethyl 2-(5-morpholin-4-ylimidazolo[5,4-b]pyridin-2-yl)acetate and

2-aminobenzenecarbonitrile, with a modified workup procedure. After quenching

with a saturated aqueous ammonium chloride solution, the two phases were

separated and the aqueous phase extracted with EtOAc. Upon standing, a solid

formed and precipitated out of the organic extracts. The precipitate, a dark brown

25 solid, was filtered off and dried. Purification by reverse phase chromatography

afforded the desired product as a reddish solid. LC/MS m/z 363.2 (MH+), R/2.20

minutes.

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Example 47

 $\label{lem:condition} \begin{tabular}{l} 4-Amino-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one \end{tabular}$

LiHMDS (3.0 eq) was added to ethyl 3*H*-imidazo[4,5-*b*]pyridin-2
ylacetate (1.0 eq) in THF at -78°C. After 20 minutes, a solution of 2-amino-6[(2*R*,6*S*)-2,6-dimethylmorpholin-4-yl]benzonitrile (1.1 eq) in THF was added. The
resulting mixture was allowed to warm to room temperature, stirred for 2 hours and
then heated to 60°C overnight. The mixture was cooled to 0°C and quenched with
an aqueous saturated NH₄Cl solution. The aqueous phase was extracted with
CH₂Cl₂ (5 times) and the organic extracts were collected, dried (Na₂SO₄), and
concentrated. The crude product was purified by HPLC. LC/MS *m*/z 391.2
(MH+), R₂ 2.35 minutes.

Example 48

Ethyl $\{5-[3-(dimethylamino)pyrrolidin-1-yl]-3H-imidazo[4,5-b]pyridin-2-yl\}acetate$

6-chloro-3-nitro-2-aminopyridine (1.0 eq) and 3-(dimethylamino)pyrrolidine (1.1 eq) were dissolved in CH₃CN and diisopropylethylamine(2.0 eq) was added. The reaction mixture was heated at 70°C overnight. The solution was cooled to room temperature, and the solvent was 20 evaporated. The residue was triturated with ether and water and dried under vacuum (LC/MS m/z 252.2 (MH+), Rt 1.09 minutes). The isolated product (1.0 eq) and 10% Pd/C (0.1 eq) were suspended in anhydrous EtOH at room temperature. The reaction flask was evacuated and subsequently filled with H2. The resulting mixture was allowed to stir under a hydrogen atmosphere overnight. Ethyl 3-ethoxy-3-iminopropanoate hydrochloride (2.0 eq) was then added and the resulting mixture was heated at reflux overnight. The solution was then filtered through Celite and evaporated under reduced pressure. The residue was suspended in CH2Cl2 and concentrated NH4OH was added until a pH of 11 was achieved. The NH4Cl thus formed was filtered off. The two phases were separated, and the 30 organic phase was dried (Na2SO4). Evaporation of the solvent and trituration of the

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residue with ether gave a light green powder. LC/MS m/z 318.1 (MH+), R 1.11 minutes.

4-Amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-3H-imidazo[4,5-b]pyridin-2-yl}quinolin-2(1H)-one

LiHMDS (3.5 eq) was added to ethyl {5-[3-(dimethylamino)pyrrolidin-1-yl]-3H-imidazo[4,5-b]pyridin-2-yl}acetate (1.0 eq) in THF at -40 °C. After 10 minutes, a solution of 2-aminobenzenecarbonitrile (1.1 eq) in THF was added. The resulting mixture was allowed to warm to room temperature, stirred for 1 h and then heated to 60 °C overnight. The mixture was cooled to room temperature and quenched with NH4Cl (aq, saturated). The aqueous phase was extracted with CH2Cl2 (5 times). The product crashes out of the organic solution during the extractions. Evaporation of the solvent under reduced pressure afforded a brown solid that was triturated repeatedly with MeOH and acetone to obtain a yellow greenish powder. LC/MS m/z 390.2 (MH+), R_t 1.48 minutes.

Example 49

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2-(4-Ethylpiperazinyl)-6-nitrobenzenecarbonitrile

2,6-Dinitrobenzenecarbonitrile (1.0 eq) and ethylpiperazine (3.6 eq) were dissolved in DMF. The resulting solution heated at 90°C for 2 hours. The solution was cooled to room temperature and poured into H_2O . A precipitate formed which was filtered to yield the desired product as a brown solid. LC/MS m/z 260.1 (MH+), R_1 1.69 minutes.

6-Amino-2-(4-ethylpiperazinyl)benzenecarbonitrile

2-(4-Ethylpiperazinyl)-6-nitrobenzenecarbonitrile (1.0 eq) was dissolved in EtOH and EtOAc. The flask was purged with N₂, and 10% Pd/C (0.1 eq) was added. The flask was evacuated and purged with H₂ three times. The resulting mixture was stirred overnight at room temperature. The mixture was filtered through Celite, and the filter pad was washed with EtOAc. The solvent was

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removed in vacuo to provide the desired product as a yellow solid. LC/MS m/z 231.2 (MH+), R 1.42 minutes.

 $\textbf{4-Amino-3-} (1 \textbf{H-benzimidazol-2-yl}) - \textbf{5-} (\textbf{4-ethylpiperazin-1-yl}) quino lin-2 \textbf{(1 \textbf{H})-one}$

t-BuLi (3.1 eq) was added to ethyl 2-benzimidazol-2-ylacetate (1.0

- eq) and 6-amino-2-(4-ethylpiperazinyl)benzenecarbonitrile (1.0 eq) in THF at 0°C. The reaction was stirred overnight. The resulting mixture was quenched with NH₄Cl (aq, saturated) and extracted with EtOAc. The combined organic layers were washed with H₂O and brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to yield a brown solid. The crude material was triturated with CH₂Cl₂ and MeOH to provide a tan solid. LC/MS *m/z* 389.1 (MH+), R₂1.80 minutes.
 - Examples 50-154

The 2-aminobenzonitriles or isatoic anhydride starting materials used to synthesize Examples 50-154 are readily recognizable by one skilled in the art. They were either commercially available or synthesized following the examples shown above (e.g. Examples 1, 2, and 49). The anhydride 6-chloro-1-(phenylmethyl)-2H-3,1-benzoxazine-2,4(1H)-dione was synthesized following the general isatoic anhydride synthesis methods described in *J. Med. Chem.* 1981, 24 (6), 735 and *J. Heterocycl. Chem.* 1975, 12(3), 565.

The benzimidazole acetates were formed by reacting aryl diamines

with ethyl 3-ethoxy-3-iminopropanoate hydrochloride as shown in Example 1. The
requisite diamines used in the syntheses are also readily recognizable by one skilled
in the art and may be synthesized following Methods 1-9. The isatoic anhydrides
were coupled with the benzimidazole acetates using methods C and D. The 2aminobenzonitriles were coupled with the benzimidazole acetates using method B,

the coupling method of example 49, or the general procedure set forth below.

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Method E

LiHMDS (3-4 eq) was added to the benzimidazole acetate (1.0 eq) in THF (at a constant temperature ranging from -78°C to 0°C). After 20 minutes, a solution of the 2-aminobenzonitrile (1.1 eq) in THF was then added. The resulting mixture was allowed to warm to room temperature, stirred for 1-3 hours and was then heated to approx. 40°C - 65°C (1 hour to 12 hours). The mixture was cooled to 0°C and quenched with NH₄Cl (aq, saturated). The aqueous phase was extracted with CH₂Cl₂ or EtOAc, and the organic extracts were collected, dried (Na₂SO₄), and filtered. Evaporation of the solvent under reduced pressure and purification of the residue by silica gel chromatography or HPLC provided the 4-amino quinolinone products.

Example	Name	LC/MS m/z (MH+)
50	4-amino-3-{5-[(3S)-3- (dimethylamino)pyrrolidin-1-yl]-1H- benzimidazol-2-yl}quinolin-2(1H)-one	389.4
51	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-6-chloroquinolin- 2(1H)-one	420
52	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-chloroquinolin- 2(1H)-one	420
53	3-(1H-benzimidazol-2-yl)-4-[(3R)-3- (dimethylamino)pyrrolidin-1-yl]quinolin- 2(1H)-one	374.2
54	3-(1H-benzimidazol-2-yl)-6-chloro-4-[(3R)- 3-(dimethylamino)pyrrolidin-1-yl]quinolin- 2(1H)-one	408.1
55	4-amino-3-[5-(4-ethylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1-methylquinolin-2(1H)- one	403.2
56	4-amino-3-(6-piperazin-1-yl-1H- benzimidazol-2-yl)quinolin-2(1H)-one	361.2
57	4-amino-3-[6-(pyridin-4-ylmethyl)-1H- benzimidazol-2-yl]quinolin-2(1H)-one	368.2
	4-amino-3-{5-[(3R,5S)-3,5- dimethylpiperazin-1-yl]-1H-benzimidazol-2- yl}quinolin-2(1H)-one	389.4

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59	4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-	075.0
	benzimidazol-2-yl]quinolin-2(1H)-one	375.2
60	4-amino-3-(6-methyl-5-morpholin-4-yl-1H-	376
61	benzimidazol-2-yl)quinolin-2(1H)-one	
O1	4-amino-3-{5-[(1-methylpiperidin-3-yl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	390.1
62	4-amino-3-{5-[(2R,6S)-2,6-	400.0
	dimethylmorpholin-4-yl]-6-fluoro-1H-	408.2
	benzimidazol-2-yl}quinolin-2(1H)-one	
63	4-amino-3-{5-[(1-methylpyrrolidin-3-yl)oxy]-	2700
	1H-benzimidazol-2-yl}quinolin-2(1H)-one	376.2
64	4-amino-3-[5-(4-methyl-1,4-diazepan-1-yl)-	200.0
•	1H-benzimidazol-2-yl]quinolin-2(1H)-one	389.2
65	4-amino-3-{5-[(3R)-3-	389.2
	(dimethylamino)pyrrolidin-1-yl]-1H-	309.2
	benzimidazol-2-yl}quinolin-2(1H)-one	
66	4-amino-6-chloro-3-{5-[(3R)-3-	423
	(dimethylamino)pyrrolidin-1-yl]-1H-	423
	benzimidazol-2-yl}quinolin-2(1H)-one	
67	ethyl {4-[2-(4-amino-2-oxo-1,2-	447.2
	dihydroquinolin-3-yl)-1H-benzimidazol-6-	441.2
	yl]piperazin-1-yl}acetate	
68	4-amino-3-{6-[methyl(1-methylpiperidin-4-	403.1
	yl)amino]-1H-benzimidazol-2-yl}quinolin-	403.1
	2(1H)-one	
69	3-[6-(4-acetylpiperazin-1-yl)-1H-	403.3
	benzimidazol-2-yl]-4-aminoquinolin-2(1H)-	400.0
	one	
70	4-amino-3-[6-(1,4'-bipiperidin-1'-yl)-1H-	443.3
	benzimidazol-2-yl]quinolin-2(1H)-one	
71	2-(4-amino-2-oxo-1,2-dihydroguinolin-3-yl)-	321.2
	1H-benzimidazole-6-carboxylic acid	
72	4-amino-5-(methyloxy)-3-[6-(4-	405.3
	methylpiperazin-1-yl)-1H-benzimidazol-2-	
	yl]quinolin-2(1H)-one	
73	4-amino-3-{6-[4-(1-methylethyl)piperazin-1-	403.3
	yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-	
	one	
74	{4-[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-	419.2
	yl)-1H-benzimidazol-6-yl]piperazin-1-	
	yl}acetic acid	
75	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-	386.1
	(1H-benzimidazol-2-yl)quinolin-2(1H)-one	
76	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	386.1
	3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one	11
77	4-amino-3-[5-(4-ethylpiperazin-1-yl)-1H-	389.1
	benzimidazol-2-yl]quinolin-2(1H)-one	

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78	4-amino-3-(5-{(2S,5S)-2-	433.3
	[(dimethylamino)methyl]-5-	
	methylmorpholin-4-yl}-1H-benzimidazol-2-	
	yl)quinolin-2(1H)-one	
79	4-amino-6-chloro-3-[5-(4-methylpiperazin-	409.2
	1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-	
	one	
80	4-amino-6-chloro-3-{5-[(3S)-3-	423.1
	(dimethylamino)pyrrolidin-1-yl]-1H-	
	benzimidazol-2-yl}quinolin-2(1H)-one	
81	4-amino-5,6-dichloro-3-{5-[(3S)-3-	457.2
	(dimethylamino)pyrrolidin-1-yl]-1H-	
1	benzimidazol-2-yl}quinolin-2(1H)-one	
82	4-amino-5,6-dichloro-3-[5-(4-	443.2
	methylpiperazin-1-yl)-1H-benzimidazol-2-	
	y[]quinolin-2(1H)-one	
83	4-amino-3-(1H-benzimidazol-2-yl)-6-	384.2
	[(pyridin-2-ylmethyl)oxy]quinolin-2(1H)-one	
84	4-amino-3-(1H-benzimidazol-2-yl)-6-	390.1
	[(2R,6S)-2,6-dimethylmorpholin-4-	4 5511
	yl]quinolin-2(1H)-one	
85	4-amino-3-(1H-benzimidazol-2-yl)-6-	362.2
	morpholin-4-ylquinolin-2(1H)-one	
86	4-amino-3-(1H-benzimidazol-2-yl)-5-[(1-	390.2
	methylpiperidin-3-yl)oxy]quinolin-2(1H)-one	
87	4-amino-3-(1H-benzimidazol-2-yl)-5-	384.1
	[(pyridin-2-ylmethyl)oxy]quinolin-2(1H)-one	
88	4-amino-3-(5-morpholin-4-yl-1H-	469.2
	benzimidazol-2-yl)-5-[(pyridin-4-	
	ylmethyl)oxy]quinolin-2(1H)-one	
89	4-amino-3-(1H-benzimidazol-2-yl)-5-	307.1
	(methyloxy)quinolin-2(1H)-one	
90	4-amino-3-(5-methyl-1H-benzimidazol-2-	321.1
	yl)-5-(methyloxy)quinolin-2(1H)-one	
· 91	4-amino-3-{5-[(2R,6S)-2,6-	420.2
	dimethylmorpholin-4-yl]-1H-benzimidazol-	
	2-yl}-5-(methyloxy)quinolin-2(1H)-one	
92	4-amino-3-(1H-benzimidazol-2-yl)-5-	362.2
	morpholin-4-ylquinolin-2(1H)-one	
93	4-amino-3-(1H-benzimidazol-2-yl)-5-	390.2
-	[(2R,6S)-2,6-dimethylmorpholin-4-	
	yl]quinolin-2(1H)-one	
94	4-amino-3-(1H-benzimidazol-2-yl)-5-(4-	375.1
٠,	methylpiperazin-1-yl)quinolin-2(1H)-one	
95	4-amino-5,6-dichloro-3-(5-morpholin-4-yl-	430
·	1H-benzimidazol-2-yl)quinolin-2(1H)-one	

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benzimidazol-2-yl}quinolin-2(1H)-one		96	3-{5-[(2-morpholin-4-ylethyl)oxy]-1H-	391.3
97	L		benzimidazol-2-yl}guinolin-2(1H)-one	391.3
11-benzimidazol-2-yl}quinolin-2(1H)-one		97	4-amino-3-{5-[(3-pyrrolidin-1-ylpmpyl)oxyl-	101
4-amino-3-(5-[(3-morpholin-4-ylpropyl)oxy]- 1H-benzimidazol-2-yl]quinolin-2(1H)-one	L		11H-benzimidazol-2-vl}quinolin-2(1H)-one	
11-Denzimidazol-2-y quinolin-2(1H)-one 4-amino-6-fluoro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]-6-fluoroquinolin-2(1H)-one 101 4-amino-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one 102 4-amino-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one 103 4-amino-3-{5-[(tetrahydrofuran-2-yl)quinolin-2(1H)-one 104 4-amino-6-fluoro-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one 105 4-amino-6-fluoro-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one 106 4-amino-3-[6-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl)quinolin-2(1H)-one 107 4-amino-3-(5-[2-(methyloxy)ethyl]oxy)-1H-benzimidazol-2-yl)quinolin-2(1H)-one 108 4-amino-3-[4-6-difluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl)quinolin-2(1H)-one 109 4-amino-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one 109 4-amino-5-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 110 4-amino-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl]quinolin-2(1H)-one 110 4-amino-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one 111 4-amino-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one 112 4-amino-6-chloro-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one 113 4-amino-6-chloro-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one 113 4-amino-6-chloro-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one 113 4-amino-6-chloro-3-(5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2-yl]-1-yl-6-fluoro-1H-benzimidazol-2-yl]quinolin-2-yl]-1-yl-6-fluoro-1H-benzimidazol-1-yl]-1-yl-6-fluoro-1H-benzimidazol-1-yl]-1-yl-6-fluoro-1H-benzimidazol-1-yl]-1-yl-6-fluoro-1H-benzimidazol-1-yl]-1-yl-6-fluoro-1H-benzimidazo		98	4-amino-3-{5-[(3-morpholin-4-vlpropyl)oxyl	120.4
4-amino-6-fluoro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	L		1H-benzimidazol-2-vl}quinolin-2(1H)-one	420.4
Denzimidazol-2-yl)quinolin-2(1H)-one		99	4-amino-6-fluoro-3-(5-morpholin-4-yl-1H	300
1-4-amino-3-{5-{3-(dimethylamino)pyrrolidin-1-y]-1H-benzimidazol-2-y }-6- fluoroquinolin-2(1H)-one			benzimidazol-2-vl)quinolin-2(1H)-one	300
1-y -1H-benzimidazol-2-y -6- fluoroquinolin-2(1H)-one		100	4-amino-3-{5-[3-(dimethylamino)pyrrolidin-	407
fluoroquinolin-2(1H)-one 101			1-yl]-1H-benzimidazol-2-yl]-6-	407
101	L		fluoroquinolin-2(1H)-one	
filuoroquinolin-2(1H)-one		101	4-amino-3-(1H-benzimidazol-2-vl)-6-	205
102	L		fluoroquinolin-2(1H)-one	295
Denzimidazol-2-yl)quinolin-2(1H)-one 103	Г	102	4-amino-3-(6-fluoro-5-morpholin-4-yl-1H	200
103	L		benzimidazol-2-vl)guinolin-2(1H)-one	300
y metny)oxy -1H-benzimidazol-2- y quinolin-2(1H)-one		103	4-amino-3-{5- (tetrahydrofuran-2-	377
104	1		yimetnyl)oxy -1H-benzimidazo -2-	377
104	L		yl}quinolin-2(1H)-one	
105 4-amino-3-[6-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one		104	4-amino-6-fluoro-3-(6-fluoro-5-morpholin-4-	398
105			yl-1H-benzimidazol-2-vl)guinolin-2(1H)-one	000
yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 4-amino-3-(5-{[2-(methyloxy)ethyl]oxy}-1H-benzimidazol-2-yl)quinolin-2(1H)-one 4-amino-3-[4,6-difluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 108		105	4-amino-3-[6-fluoro-5-(4-methylpiperazin-1-	393
one 106			yr)-1H-benzimidazol-2-yl]quinolin-2(1H)-	000
107	\vdash		one	
107		106	4-amino-3-(5-{[2-(methyloxy)ethyl]oxy}-1H-	351
107 4-amino-3-[4,6-difluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	<u> </u>	40=		
methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 108	1	107	4-amino-3-[4,6-difluoro-5-(4-	411
108 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}-5- fluoroquinolin-2(1H)-one 109 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 110 4-amino-5-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 111 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one 112 4-amino-5-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}			metnylpiperazin-1-yl)-1H-benzimidazol-2-	1
1-yl]-1H-benzimidazol-2-yl]-5- fluoroquinolin-2(1H)-one 109	\vdash	400	_lyi]quinolin-2(1H)-one	
109 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 110 4-amino-5-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 111 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one 112 4-amino-5-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-		108	4-amino-3-{5-[3-(dimethylamino)pyrrolidin-	407.1
4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 110 4-amino-5-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one 111 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one 112 4-amino-5-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-			1-ylj-1H-DenZimidazol-2-yl}-5-	
yl)-1H-benzimidazol-2-yl]quinolin-2(1H)- one 110 4-amino-5-chloro-3-[5-(4-methylpiperazin- 1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)- one 111 4-amino-3-{5-[3-(dimethylamino)pyrrolidin- 1-yl]-6-fluoro-1H-benzimidazol-2- yl}quinolin-2(1H)-one 112 4-amino-5-chloro-3-{5-[3- (dimethylamino)pyrrolidin-1-yl]-1H- benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3- (dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-	├	100	lluoroquinolin-2(1H)-one	
110 4-amino-5-chloro-3-[5-(4-methylpiperazin- 1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)- one 111 4-amino-3-{5-[3-(dimethylamino)pyrrolidin- 1-yl]-6-fluoro-1H-benzimidazol-2- yl}quinolin-2(1H)-one 112 4-amino-5-chloro-3-{5-[3- (dimethylamino)pyrrolidin-1-yl]-1H- benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3- (dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-		109	4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-	393.1
4-amino-5-chloro-3-[5-(4-methylpiperazin- 1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)- one 4-amino-3-{5-[3-(dimethylamino)pyrrolidin- 1-yl]-6-fluoro-1H-benzimidazol-2- yl}quinolin-2(1H)-one 4-amino-5-chloro-3-{5-[3- (dimethylamino)pyrrolidin-1-yl]-1H- benzimidazol-2-yl}quinolin-2(1H)-one 4-amino-6-chloro-3-{5-[3- (dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-			lone	
1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)- one 111	\vdash	110		
111 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one 112 4-amino-5-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-		110	4-anino-5-chioro-3-[5-(4-methylpiperazin-	409.1
4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one 112 4-amino-5-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-			one In-benzimidazol-2-yl]quinolin-2(1H)-	
1-yl]-6-fluoro-1H-benzimidazol-2- yl}quinolin-2(1H)-one 112	-	111		
yl}quinolin-2(1H)-one 112			11-vil-6 fluoro 111 hamaini 1	407.1
112 4-amino-5-chloro-3-{5-[3- 423.1 (dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3- 441 (dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-			Wildwindin 2(1H) one	
(dimethylamino)pyrrolidin-1-yl]-1H- benzimidazol-2-yl}quinolin-2(1H)-one 113 4-amino-6-chloro-3-{5-[3- (dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-		112	4-amino-5-chloro 2 (5 to	
113 4-amino-6-chloro-3-{5-[3- 441 (dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-			(dimethylamino)	423.1
441 (dimethylamino)pyrrolidin-1-yll-6-fluoro-1H-		•	benzimidazol-2-vlauinalia ozatu	
(dimethylamino)pyrrolidin-1-yll-6-fluoro-1H-		113	4-amino-6-chloro 2 (5 fo	
benzimidazol-2-yl}quinolin-2(1H)-one			(dimethylamino)nymolidia 4	441
-2-11-inidazor-z-yiyquiiloiin-z(1H)-one		j	benzimidazol-2-vilguinglis 2/411) a a a	

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114	4-amino-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	391.2
115	4-amino-3-(6-thiomorpholin-4-yl-1H- benzimidazol-2-yl)quinolin-2(1H)-one	378.4
116	4-amino-3-[5-(4-cyclohexylpiperazin-1-yl)- 1H-benzimidazol-2-yl]quinolin-2(1H)-one	443.1
117	4-amino-3-{6-[3-(diethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	417.1
118	4-amino-3-[6-(4-pyridin-2-ylpiperazin-1-yl)- 1H-benzimidazol-2-yl]quinolin-2(1H)-one	438.3
119	4-amino-3-[5-(4-methylpiperazin-1-yl)-3H- imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)- one	376.3
120	4-amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one	410.2
121	2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)- N-methyl-N-(1-methylpiperidin-4-yl)-1H- benzimidazole-5-carboxamide	431.3
122	4-amino-3-(5-{[4-(1-methylethyl)piperazin- 1-yl]carbonyl}-1H-benzimidazol-2- yl)quinolin-2(1H)-one	431.3
123	4-amino-3-[5-(4-methylpiperazin-1-yl)-1H- benzimidazol-2-yl]-6-nitroquinolin-2(1H)- one	420.2
124	4-amino-3-[5-(1,4'-bipiperidin-1'- ylcarbonyl)-1H-benzimidazol-2-yl]quinolin- 2(1H)-one	471.1
125	4-amino-3-{5-[(4-methylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	403.3
126	4-amino-3-[5-(1-oxidothiomorpholin-4-yl)- 1H-benzimidazol-2-yl]quinolin-2(1H)-one	394.5
127	3-{5-[(4-acetylpiperazin-1-yl)carbonyl]-1H- benzimidazol-2-yl}-4-aminoquinolin-2(1H)- one	431.3
128	4-amino-3-(5-{[(3R)-3- (dimethylamino)pyrrolidin-1-yl]carbonyl}- 1H-benzimidazol-2-yl)quinolin-2(1H)-one	417.4

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129	4-amino-3-(5-{[(3S)-3-	417.4
	(dimethylamino)pyrrolidin-1-yl]carbonyl}-	
	1H-benzimidazol-2-yl)quinolin-2(1H)-one	
130	4-amino-3-(5-{[4-(dimethylamino)piperidin-	431.4
	1-yl]carbonyl}-1H-benzimidazol-2-	701.4
	yl)quinolin-2(1H)-one	
131	methyl 2-(4-amino-5-fluoro-2-oxo-1,2-	050.0
1	dihydroquinolin-3-yl)-1H-benzimidazole-6-	353.2
İ	carboxylate	
132		
132	4-amino-3-[5-(1,3'-bipyrrolidin-1'-yl)-1H-	415.5
	benzimidazoi-2-yl]quinolin-2(1H)-one	
133	4-amino-3-[5-(pyridin-3-yloxy)-1H-	370.2
	benzimidazol-2-yl]quinolin-2(1H)-one	370.2
_	July 2012 Jijquilloini-2(111)-offe	i
134	4-amino-5,6-bis(methyloxy)-3-[5-(4-	435.5
	methylpiperazin-1-yl)-1H-benzimidazol-2-	100.0
	yl]quinolin-2(1H)-one	
135	2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-	405.3
	N-[2-(dimethylamino)ethyl]-N-methyl-1H-	405.5
	benzimidazole-5-carboxamide	
136	2-(4-amino-2-oxo-1;2-dihydroquinolin-3-yl)-	447.0
.00	N-methyl-N-(1-methylpyrrolidin-3-yl)-1H-	417.2
	benzimidozolo E corbovomidin-3-yr)-1H-	
137	benzimidazole-5-carboxamide	
107	4-amino-3-{5-[(5-methyl-2,5-	415.2
	diazabicyclo[2.2.1]hept-2-yl)carbonyl]-1H-	
138	benzimidazol-2-yl}quinolin-2(1H)-one	
130	4-amino-3-{5-[(4-cyclohexylpiperazin-1-	471.6
	yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-	
	2(1H)-one	
139	4-amino-3-{5-[(2-piperidin-1-ylethyl)amino]-	403.2
	1H-benzimidazol-2-yl}quinolin-2(1H)-one	
140	ethyl 4-{[2-(4-amino-2-oxo-1,2-	447.3
	dihydroquinolin-3-yl)-1H-benzimidazol-5-	
	yl]amino)piperidine-1-carboxylate	
141	4-amino-3-[5-({(5R)-5-	405.2
	[(methyloxy)methyl]pyrrolidin-3-yl}amino)-	403.2
	1H-benzimidazol-2-y[]quinolin-2(1H)-one	
142	4-amino-3-{5-[(pyridin-2-ylmethyl)amino]-	000.0
	1H-henzimidazal 2 vi) avinalia 2/1Li) and	383.3
	1H-benzimidazol-2-yl}quinolin-2(1H)-one	İ
143	4-amino-3-[5-(piperidin-3-ylamino)-1H-	375.2
	benzimidazol-2-yl]quinolin-2(1H)-one	3/3.2
	- Sizimidazor-z-yijquiiloliii-z(117)-one	1
144	4-amino-5-fluoro-3-{5-[(pyridin-2-	404.0
• • •	ylmethyl)amino]-1H-benzimidazol-2-	401.3
	yl}quinolin-2(1H)-one	••
	13-34-au-out-5(111)-0116	

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151 152	4-amino-3-(5-thien-2-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N,N-dimethyl-1H-benzimidazole-5-	359.2 384.1
	3-yl)-1H-benzimidazole-5-carboxamide 4-amino-3-(5-thien-2-yl-1H-benzimidazol-2-	
149	4-amino-3-(5-bromo-1H-benzimidazol-2-yl)quinolin-2(1H)-one N,N-dimethyl-2-(2-oxo-1,2-dihydroquinolin-	357.1 333.1
148	4-amino-3-(1H-benzimidazol-2-yl)-7- bromoquinolin-2(1H)-one	357.1
147	4-amino-3-(1H-benzimidazol-2-yl)-6- bromoquinolin-2(1H)-one	357.1
146	4-amino-5-fluoro-3-[5-(piperidin-3-ylamino)- 1H-benzimidazol-2-yl]quinolin-2(1H)-one	393.3
145	ethyl 4-{[2-(4-amino-5-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-5-yl]amino}piperidine-1-carboxylate	465.5

Examples 155-270

Examples 155 to 270 shown in the following Table were synthesized using the methods described above such as Methods 1-15 and those set forth in the Schemes and other Examples or modified as apparent to one of reasonable skill in the art using commercially available materials.

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Example	Name	1.0/110
LXample	Name .	LC/MS m/z (MH+)
155	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-7-chloro-6- iodoquinolin-2(1H)-one	547
156	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-nitroquinolin- 2(1H)-one	431
157	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- • 3-(1H-benzimidazol-2-yl)-6-methylquinolin-2(1H)-one	401
158	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6,7- difluoroquinolin-2(1H)-one	422
159	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-7-chloroquinolin- 2(1H)-one	421
160	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-bromoquinolin- 2(1H)-one	465
161	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-2-oxo-1,2- dihydroquinoline-6-carbonitrile	411
162	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-fluoroquinolin- 2(1H)-one	404
163	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-6,7- bis(methyloxy)quinolin-2(1H)-one	447
164	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6,7- dichloroquinolin-2(1H)-one	455
165	1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-4-carboxamide	531
	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-6-fluoro-7-[(3- hydroxypropyl)amino]quinolin-2(1H)-one	478
	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-7-(dimethylamino)- 6-fluoroquinolin-2(1H)-one	448
168	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-5-fluoroquinolin- 2(1H)-one	404

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169	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-(4-	508
	nitrophenyl)quinolin-2(1H)-one	
170	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-7-{[2- (dimethylamino)ethyl]amino}-6-	491
	fluoroquinolin-2(1H)-one	
171	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-6-fluoro-7-(1H- imidazol-1-yl)quinolin-2(1H)-one	471
172	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-[4- (methyloxy)phenyl]quinolin-2(1H)-one	493
173	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-6-fluoro-7- morpholin-4-ylquinolin-2(1H)-one	490
174	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 6,7-difluoro-3-(3H-imidazo[4,5-b]pyridin-2- yl)quinolin-2(1H)-one	423
175	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-(3- nitrophenyl)quinolin-2(1H)-one	508
176	1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-3-carboxamide	531
177	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-5-methylquinolin- 2(1H)-one	401
178	6-(3-acetylphenyl)-4-[(3R)-1- azabicyclo[2.2.2]oct-3-ylamino]-3-(3H- imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)- one	506
179	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-5-chloroquinolin- 2(1H)-one	421
180	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 6-fluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)- 7-morpholin-4-ylquinolin-2(1H)-one	491
181	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-7- (cyclopropylamino)-6-fluoroquinolin-2(1H)- one	460
182	N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide	521

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183	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3 (1H-benzimidazol-2-yl)-6-fluoro-7-(4-	503
	methylpiperazin-1-yl)quinolin-2(1H)-one	
184	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 6-fluoro-7-(1H-imidazol-1-yl)-3-(3H-	472
	imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	
185		
100	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3- (1H-benzimidazol-2-yl)-6-fluoro-7-[(2-	525
	pyridin-2-ylethyl)amino]quinolin-2(1H)-one	
186	4-[(3S)-1-azabicyclo[2.2.2]oct-3-vlamino]-3-	488
	(1H-benzimidazol-2-yl)-6-fluoro-7-piperidin- 1-ylquinolin-2(1H)-one	
187	6-chloro-3-(3H-imidazo[4,5-b]pyridin-2-	000
	yl)quinolin-2(1H)-one	298
188	ethyl 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-	560
	ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-	
	2-oxo-1,2-dihydroquinolin-7-yl]piperidine-4- carboxylate	
189	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	519
	3-(1H-benzimidazol-2-yl)-6-(1-benzothien-	313
	2-yl)quinolin-2(1H)-one	
190	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-	474
	(1H-benzimidazol-2-yl)-6-fluoro-7-	7/7
	pyrrolidin-1-ylquinolin-2(1H)-one	
191	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	532
	3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-	302
	(trifluoromethyl)phenyl]quinolin-2(1H)-one	
192	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	494
	3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-	70-7
	(methyloxy)phenyl]quinolin-2(1H)-one	
193	ethyl 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-	560
	ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-	000
	2-oxo-1,2-dihydroquinolin-7-yl]piperidine-3-	İ
	carboxylate	
194	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	491
	3-(1H-benzimidazol-2-yl)-6-(4-	701
	ethylphenyl)quinolin-2(1H)-one	
195	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-	476
	(1H-benzimidazol-2-yl)-6-fluoro-7-[(2-	470
	methylpropyl)amino]quinolin-2(1H)-one	İ
196	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	401
	3-(1H-benzimidazol-2-yl)-5-methylquinolin-	401
	2(1H)-one	
197	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	520
	6-(2,4-dichlorophenyl)-3-(3H-imidazo[4,5-	532
	b]pyridin-2-yl)quinolin-2(1H)-one	•
	i zipyriani z yryquirioliri-2(ITI)-one	

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198	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]- 3-(1H-benzimidazol-2-yl)-6-[3-	531
Ì	(trifluoromethyl)phenyl]quinolin-2(1H)-one	
199	3-(1H-benzimidazol-2-yl)-4-	305
155	(dimethylamino)quinolin-2(1H)-one	303
200	4-hydroxy-3-(1H-imidazo[4,5-f]quinolin-2-	329
200	yl)quinolin-2(1H)-one	023
201	4-hydroxy-3-(1H-imidazo[4,5-b]pyridin-2-	279
20.	yl)quinolin-2(1H)-one	2.0
202	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	525
	ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-	
	2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid	
203	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	524
	ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-	
	2-oxo-1,2-dihydroquinolin-6-yl]benzamide	-
204	N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	538
	ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-	
	2-oxo-1,2-dihydroquinolin-6-	
	yl]phenyl}acetamide	
205	3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	525
	ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-	
200	2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid	FOE
206	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	525
	ylamino]-3-(1H-benzimidazol-2-yl)-7-fluoro- 2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid]
207	N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	538
201	ylamino]-3-(1H-benzimidazoi-2-yl)-7-fluoro-	300
	2-oxo-1,2-dihydroquinolin-6-	
	yl]phenyl}acetamide	
208	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	511
	3-(1H-benzimidazol-2-yl)-7-chloro-6-(2-	
	methylphenyl)quinolin-2(1H)-one	
209	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	411
	3-(1H-benzimidazol-2-yl)-2-oxo-1,2-	
	dihydroquinoline-7-carbonitrile	
210	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	417
	3-(1H-benzimidazol-2-yl)-7-	
	(methyloxy)quinolin-2(1H)-one	
211	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	506
	ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-	
040	1,2-dihydroquinolin-7-yl]benzamide	404
212	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	434
	3-(1H-benzimidazol-2-yl)-6-fluoro-7-	
040	(methyloxy)quinolin-2(1H)-one	164
213	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	464
•	3-(1H-benzimidazol-2-yl)-6-chloro-7-	
·	(dimethylamino)quinolin-2(1H)-one	

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044	LA EXODA A	
214	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	555
1	3-(1H-benzimidazol-2-yl)-7-	
	(dimethylamino)-6-iodoquinolin-2(1H)-one	1_
215	3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	573
	ylamino]-3-(1H-benzimidazol-2-yl)-7-(1H-	
	imidazol-1-yl)-2-oxo-1,2-dihydroguinolin-6-	
	yl]benzoic acid	
216	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-	590
	ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-7.	.
	piperidin-1-yl-1,2-dihydroquinolin-6-	
	yl]benzoic acid	
217	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	571
	3-(1H-benzimidazol-2-yl)-7-(methyloxy)-6-	, ,,,
	[4-(methylsulfonyl)phenyl]quinolin-2(1H)-	
	one	
218	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	401
	3-(1H-benzimidazol-2-yl)-8-methylquinolin-	101
L	_ 2(1H)-one	
219	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-	422
	(1H-benzimidazol-2-yl)-6,7-difluoroquinolin-	122
	2(1H)-one	
220	3-(1H-benzimidazol-2-yl)-6-methyl-4-	374
	(piperidin-3-ylamino)quinolin-2(1H)-one	
221	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-	493
	(1H-benzimidazol-2-yl)-6-[2-	
	(methyloxy)phenyl]quinolin-2(1H)-one	·
222	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-	493
	(1H-benzimidazol-2-yl)-6-[3-	100
	(methyloxy)phenyl]quinolin-2(1H)-one	
223	3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-	396
L	(piperidin-4-ylamino)quinolin-2(1H)-one	000
224	3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-	382
	(pyrrolidin-3-ylamino)quinolin-2(1H)-one	302
225	3-(1H-benzimidazol-2-yl)-6-chloro-4-[(3-	439
1	morpholin-4-ylpropyl)amino]quinolin-2(1H)-	409
	one	
226	6-chloro-3-(5-morpholin-4-yl-1H-	480
	benzimidazol-2-yl)-4-(piperidin-4-	400
	ylamino)quinolin-2(1H)-one	
227	6-chloro-3-(5-morpholin-4-yl-1H-	494
	benzimidazol-2-yi)-4-[(piperidin-2-	494
	ylmethyl)amino]quinolin-2(1H)-one	
228	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-	F0C
	chloro-3-(5-morpholin-4-yi-1H-	506
	benzimidazol 2 vl\quinelin 2/41\\ ana	
	benzimidazol-2-yl)quinolin-2(1H)-one	

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229	6-chloro-3-(5-morpholin-4-yl-1H-	480
223	benzimidazol-2-yl)-4-(piperidin-3-	700
230	ylamino)quinolin-2(1H)-one	400
230	6-chloro-4-{[2-(dimethylamino)ethyl]amino}-	468
Ì	3-(5-morpholin-4-yl-1H-benzimidazol-2-	
	yl)quinolin-2(1H)-one	
231	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-	506
	6-chloro-3-(5-morpholin-4-yl-1H-	
	benzimidazol-2-yl)quinolin-2(1H)-one	·
232	6-chloro-3-(5-morpholin-4-yl-1H-	494
	benzimidazol-2-yl)-4-[(piperidin-3-	
	ylmethyl)amino]quinolin-2(1H)-one	
233	6-chloro-3-(5-morpholin-4-yl-1H-	494
	benzimidazol-2-yl)-4-[(piperidin-4-	
	ylmethyl)amino]quinolin-2(1H)-one	
234	4-{[(1R,2R)-2-aminocyclohexyl]amino}-6-	494
201	chloro-3-(5-morpholin-4-yl-1H-	404
}	benzimidazol-2-yl)quinolin-2(1H)-one	
235	4-[(4-aminocyclohexyl)amino]-6-chloro-3-	494
233	(5-morpholin-4-yl-1H-benzimidazol-2-	494
220	yl)quinolin-2(1H)-one	400
236	4-{[(2S)-2-amino-3-methylbutyl]amino}-6-	482
	chloro-3-(5-morpholin-4-yl-1H-	
	benzimidazol-2-yl)quinolin-2(1H)-one	
237	4-({[4-(aminomethyl)phenyl]methyl}amino)-	516
	6-chloro-3-(5-morpholin-4-yl-1H-	
	benzimidazol-2-yl)quinolin-2(1H)-one	
238	6-chloro-3-(5-morpholin-4-yl-1H-	480
	benzimidazol-2-yl)-4-[(pyrrolidin-2-	
	ylmethyl)amino]quinolin-2(1H)-one	
239	4-{[(1R)-1-(aminomethyl)propyl]amino}-6-	468
	chloro-3-(5-morpholin-4-yl-1H-	
	benzimidazol-2-yl)quinolin-2(1H)-one	
240	4-{[(1S)-2-amino-1-	530
	(phenylmethyl)ethyl]amino}-6-chloro-3-(5-	
	morpholin-4-yl-1H-benzimidazol-2-	
	yl)quinolin-2(1H)-one	
241	6-chloro-4-{[3-(4-methylpiperazin-1-	537
	yl)propyl]amino}-3-(5-morpholin-4-yl-1H-	00.
	benzimidazol-2-yl)quinolin-2(1H)-one	
242	6-chloro-3-(5-morpholin-4-yl-1H-	570
242	benzimidazol-2-yl)-4-{[1-	5/0
	(nbonylmothyl)ninoridin 4	1
•	(phenylmethyl)piperidin-4-	
	yl]amino}quinolin-2(1H)-one	
243	6-chloro-3-(5-morpholin-4-yl-1H-	524
	benzimidazol-2-yl)-4-[(3-morpholin-4-	ł
	ylpropyl)amino]quinolin-2(1H)-one	

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244	6-chloro-3-(5-morpholin-4-yl-1H-	508
	benzimidazol-2-yl)-4-[(2-piperidin-1-	
	ylethyl)amino]quinolin-2(1H)-one	1
245	6-chloro-3-(5-morpholin-4-yl-1H-	488
	benzimidazol-2-yl)-4-[(pyridin-3-	100
	ylmethyl)amino]quinolin-2(1H)-one	
246	6-chloro-4-{[3-(1H-imidazol-1-	505
	yl)propyl]amino}-3-(5-morpholin-4-yl-1H-	. 303
	benzimidazol-2-yl)quinolin-2(1H)-one	
247	6-chloro-3-(5-morpholin-4-yl-1H-	488
	benzimidazol-2-yl)-4-[(pyridin-4-	488
	ylmethyl)amino]quinolin-2(1H)-one	1
248	6-chloro-4-{[2-(methylamino)ethyl]amino}-	151
	3-(5-morpholin-4-yl-1H-benzimidazol-2-	454
	yl)quinolin-2(1H)-one	}
249	6 chloro 4 (((2) mothed 4 minut 1) 4 4 4 4	
2.40	6-chloro-4-{[(2-methyl-1-piperidin-4-yl-1H-	624
	benzimidazol-5-yl)methyl]amino}-3-(5-	
	morpholin-4-yl-1H-benzimidazol-2-	
250	yl)quinolin-2(1H)-one	
250	6-chloro-3-(5-morpholin-4-yl-1H-	494
	benzimidazol-2-yl)-4-[(2-pyrrolidin-1-	
251	ylethyl)amino]quinolin-2(1H)-one	
251	6-chloro-3-(5-morpholin-4-yl-1H-	466
	benzimidazol-2-yl)-4-(pyrrolidin-3-	
050	ylamino)quinolin-2(1H)-one	
252	4-{[(1R,2R)-2-aminocyclohexyl]amino}-6-	507
•	chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	
	benzimidazol-2-yl]quinolin-2(1H)-one	
253	4-[(4-aminocyclohexyl)amino]-6-chloro-3-	507
	[5-(4-methylpiperazin-1-yl)-1H-	
	benzimidazol-2-yl]quinolin-2(1H)-one	
254	4-({[4-(aminomethyl)phenyl]methyl}amino)-	529
	6-chloro-3-[5-(4-methylpiperazin-1-vl)-1H-	
	benzimidazol-2-yl]quinolin-2(1H)-one	
255	6-chloro-4-{[2-(methylamino)ethylamino}-	467
	3-[5-(4-methylpiperazin-1-yl)-1H-	101
	benzimidazol-2-yl]quinolin-2(1H)-one	
256	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	550
	benzimidazol-2-yl]-4-{[3-(4-	550
	methylpiperazin-1-yl)propyl]amino}quinolin-	
	2(1H)-one	
257	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	F00'
	benzimidazol-2-yi]-4-{[1-	583`
	(phenylmethyl)piperidin-4-	
	yl]amino}quinolin-2(1H)-one	•
	yyanınoyquirioliii-z(IH)-one	

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258	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	507
	benzimidazol-2-yl]-4-[(2-pyrrolidin-1-	
	ylethyl)amino]quinolin-2(1H)-one	
259	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	479
	benzimidazol-2-yl]-4-(pyrrolidin-3-	
	ylamino)quinolin-2(1H)-one	
260	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	493
	benzimidazol-2-yl]-4-(piperidin-4-	
	ylamino)quinolin-2(1H)-one	
261	6-chloro-3-(5-morpholin-4-yl-1H-	508
	benzimidazol-2-yl)-4-[(2-piperidin-2-	
	ylethyl)amino]quinolin-2(1H)-one	
262	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-7-	506
	chloro-3-(5-morpholin-4-yl-1H-	
	benzimidazol-2-yl)quinolin-2(1H)-one	
263	7-chloro-3-(5-morpholin-4-yl-1H-	480
	benzimidazol-2-yl)-4-(piperidin-3-	
	ylamino)quinolin-2(1H)-one	
264	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	507
	benzimidazol-2-yl]-4-[(piperidin-2-	
	ylmethyl)amino]quinolin-2(1H)-one	
265	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	493
	benzimidazol-2-yl]-4-{[(2S)-pyrrolidin-2-	
	ylmethyl]amino}quinolin-2(1H)-one	· ·
266	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-	493
	benzimidazol-2-yl]-4-{[(2R)-pyrrolidin-2-	
	ylmethyl]amino}quinolin-2(1H)-one	
267	6-chloro-4-({[(2S)-1-ethylpyrrolidin-2-	521
	yl]methyl}amino)-3-[5-(4-methylpiperazin-1-	
	yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-	
	one	
268	6-chloro-4-({[(2R)-1-ethylpyrrolidin-2-	521
	yl]methyl}amino)-3-[5-(4-methylpiperazin-1-	
	yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-	
	one	
269	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-	493
	(1H-benzimidazol-2-yl)-6-[4-	
	(methyloxy)phenyl]quinolin-2(1H)-one	
270	6-(3-aminophenyl)-4-[(3S)-1-	478
	azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-	
<u></u>	benzimidazol-2-yl)quinolin-2(1H)-one	

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Assay Procedures

In vitro kinase assays for receptor tyrosine kinases

The kinase activity of various protein tyrosine kinases can be measured by providing ATP and a suitable peptide or protein tyrosine-containing substrate, and assaying the transfer of phosphate moiety to the tyrosine residue. 5 Recombinant proteins corresponding to the cytoplasmic domains of the flt-1 (VEGFR1), KDR (VEGFR2), and bFGF receptors were expressed in Sf9 insect cells using a Baculovirus expression system (InVitrogen) and purified via Glu antibody interaction (for Glu-epitope tagged constructs) or by Metal Ion Chromatography (for Hiss tagged constructs). For each assay, test compounds were 10 serially diluted in DMSO then mixed with an appropriate kinase reaction buffer plus ATP. Kinase protein and an appropriate biotinylated peptide substrate were added to give a final volume of 100 μ L, reactions were incubated for 1-2 hours at room temperature and stopped by the addition of 50 µL of 45 mM EDTA, 50 mM Hepes 15 pH 7.5. Stopped reaction mix (75 µL) was transferred to a streptavidin coated microtiter plate (Boehringer Mannheim) and incubated for 1 hour. Phosphorylated peptide product was measured with the DELFIA time-resolved fluorescence system (Wallac), using a Eu-labeled anti-phosphotyrosine antibody PT66 with the modification that the DELFIA assay buffer was supplemented with 1 mM MgCl2 for 20 the antibody dilution. Time resolved fluorescence was read on a Wallac 1232 DELFIA fluorometer. The concentration of each compound for 50% inhibition (IC50) was calculated by non-linear regression using XL Fit data analysis software.

Flt-1, KDR, and bFGFR kinases were assayed in 50 mM Hepes pH 7.0, 2 mM MgCl₂, 10 mM MnCl₂, 1 mM NaF, 1 mM DTT, 1 mg/ml BSA, 2 μM ATP, and 0.42 μM biotin-GGGGQDGKDYIVLPI-NH₂. Flt-1, KDR, and bFGFR kinases were added at 0.1 μg/mL, 0.05 μg/mL, or 0.1 μg/mL respectively.

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Each of the following compounds was synthesized and assayed using the procedures described above: 3-{5-[2-(ethylanilino)ethoxy]-1H-benzimidazol-2-yl}-4-hydroxy-2(1H)-quinolinone: 3-[5-(4-aminophenoxy)-1H-benzimidazol-2-yl]-4-hydroxy-2(1H)-quinolinone; 3-{6-5 [[2-(dimethylamino)ethyl](methyl)amino]-1H-benzimidazol-2-yl}-4-hydroxy-2(1H)quinolinone; 4-hydroxy-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)quinolinone; 3-[5-(3-amino-1-pyrrolidinyl)-1H-benzimidazol-2-yl]-4-hydroxy-2(1H)quinolinone; N,N-dimethyl-2-(2-oxo-1,2-dihydro-3-quinolinyl)-1H-benzimidazole-5carboxamide; 3-{5-[2-(4-morpholinyl)ethoxy]-1H-benzimidazol-2-yl}-2(1H)-10 quinolinone; 3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2-yl}-2(1H)quinolinone; 3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydro-4-quinolinecarbonitrile; 4-amino-3-{5-[2-(4-morpholinyl)ethoxyl-1H-benzimidazol-2-yl}-2(1H)-quinolinone: 4-amino-3-[6-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-[6-(3-amino-1-pyrrolidinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 2-(4-15 amino-2-oxo-1,2-dihydro-3-quinolinyl)-1H-benzimidazole-5-carbonitrile; 2-(4amino-2-oxo-1,2-dihydro-3-quinolinyl)-N,N-dimethyl-1H-benzimidazole-5carboxamide; 4-amino-3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2yl}-2(1H)-quinolinone; 2-(4-amino-2-oxo-1,2-dihydro-3-quinolinyl)-1Hbenzimidazole-6-carboximidamide; 4-amino-3-[5-(4-morpholinylcarbonyl)-1H-20 benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-[5-(1H-1,2,4-triazol-1-yl)-1Hbenzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-[5-(dimethylamino)-1Hbenzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-[5-(1-piperidinyl)-1Hbenzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-[5-(2-thjenyl)-1H-benzimidazol-2yl]-2(1H)-quinolinone; 4-amino-3-{5-[3-(1-pyrrolidinyl)propoxy]-1H-benzimidazol-25 2-yl}-2(1H)-quinolinone; 4-amino-3-{5-[3-(4-morpholinyl)propoxy]-1Hbenzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-3-[5-(3,5-dimethyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-[5-(2,6-dimethyl-4morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-[5-(4-methyl-1piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-(1H-

benzimidazol-2-yl)-6-[hydroxy(oxido)amino]-2(1H)-quinolinone; 4-amino-3-(1H-

benzimidazol-2-yl)-5-[2-(4-morpholinyl)ethoxy]-2(1H)-quinolinone; 4-amino-3-(1H-

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benzimidazol-2-yl)-6-(4-methyl-1-piperazinyl)-2(1H)-quinolinone; 4-amino-3-(1Hbenzimidazol-2-yl)-5-[(1-methyl-3-piperidinyl)oxy]-2(1H)-quinolinone; 4-amino-6chloro-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-6chloro-3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2-yl}-2(1H)quinolinone; 4-amino-6-[hydroxy(oxido)amino]-3-{5-[2-(4-morpholinyl)ethoxy]-1H-5 benzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-5-[2-(4-morpholinyl)ethoxy]-3-{5-[2-(4-morpholinyl)ethoxy]-1H-benzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-3-(1H-benzimidazol-2-yl)-6-(2-pyridinylmethoxy)-2(1H)-quinolinone; 4-amino-6fluoro-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2-yl}-6-fluoro-2(1H)-10 quinolinone; 3-(1H-benzimidazol-2-yl)-4-[(tetrahydro-2-furanylmethyl)amino]-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(methylamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(ethylamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2yl)-4- $\{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino\}-2(1H)-quinolinone; 3-(1H-methyl-2-pyrrolidinyl)ethyl]amino\}-2(1H)-quinolinone; 3-(1H-methyl-2-pyrrolidinyl)ethyl]amino}$ benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]-2(1H)-quinolinone; 3-(1H-15 benzimidazol-2-yl)-4-(4-fluoroanilino)-2(1H)-quinolinone; 4-(1azabicyclo[2.2.2]oct-3-ylamino)-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(1H-benzimidazol-6-ylamino)-2(1H)-quinolinone; 4anilino-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(methoxyamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-5ylmethyl)amino]-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(4morpholinylamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-hydrazino-2(1H)-quinolinone; 4-(1-azabicyclo[2.2.2]oct-3-ylamino)-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 4-(1-azabicyclo[2.2.2]oct-3-ylamino)-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 4-[(2-methoxyethyl)amino]-3-[6-(4-morpholinyl)-1Hbenzimidazol-2-yl]-2(1H)-quinolinone; 4-[(2-hydroxyethyl)amino]-3-[5-(4morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-(methoxyamino)-3-[5-(4morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 3-[5-(4-morpholinyl)-1Hbenzimidazol-2-yl]-4-(3-piperidinylamino)-2(1H)-quinolinone; 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]-2(1H)-quinolinone; 4-{[2-

(dimethylamino)ethyl]amino}-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-

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quinolinone; 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(tetrahydro-2furanylmethyl)amino]-2(1H)-quinolinone; 4-{[2-(methylamino)ethyl]amino}-3-[5-(4morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 3-[5-(4-morpholinyl)-1Hbenzimidazol-2-yl]-4-(3-pyrrolidinylamino)-2(1H)-quinolinone; 4-[(2-amino-4-5 methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)quinolinone; 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1Hbenzimidazol-2-yl]-2(1H)-quinolinone; 3-(5,6-dimethyl-1H-benzimidazol-2-yl)-4-(3piperidinylamino)-2(1H)-quinolinone; 4-[(2-aminocyclohexyl)amino]-3-[5-(4morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone: 4-[(2-10 aminocyclohexyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)quinolinone; 3-(1H-benzimidazol-2-yl)-4-hydroxybenzo[g]quinolin-2(1H)-one; 4amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-amino-3-(5morpholin-4-yl-3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-amino-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-15 2(1H)-one; 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-3H-imidazo[4,5b]pyridin-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6chloroquinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6chloro-4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]quinolin-2(1H)-one; 4-amino-3-[5-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1-methylquinolin-2(1H)-one; 4amino-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[6-(pyridin-4-ylmethyl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4amino-3-(6-methyl-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4amino-3-{5-[(1-methylpiperidin-3-yl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)one; 4-amino-3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-6-fluoro-1H-

benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(1-methylpyrrolidin-3-

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yl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[5-(4-methyl-1,4diazepan-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4amino-6-chloro-3-{5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2yl}quinolin-2(1H)-one; ethyl {4-[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-5 benzimidazol-6-yl]piperazin-1-yl}acetate; 4-amino-3-{6-[methyl(1-methylpiperidin-4-yl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 3-[6-(4-acetylpiperazin-1yl)-1H-benzimidazol-2-yl]-4-aminoquinolin-2(1H)-one; 4-amino-3-[6-(1,4'bipiperidin-1'-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylic acid; 4-amino-5-(methyloxy)-10 3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{6-[4-(1-methylethyl)piperazin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; {4-[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-6-yl]piperazin-1yl}acetic acid; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-15 yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[5-(4-ethylpiperazin-1-yl)-1Hbenzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(5-{(2S,5S)-2-[(dimethylamino)methyl]-5-methylmorpholin-4-yl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-20 yl]quinolin-2(1H)-one; 4-amino-6-chloro-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-5,6-dichloro-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4amino-5,6-dichloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-[(pyridin-2-ylmethyl)oxy]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-[(2R,6S)-2,6-dimethylmorpholin-4-25 yl]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-morpholin-4ylquinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-[(1-methylpiperidin-3yl)oxy]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-[(pyridin-2ylmethyl)oxy]quinolin-2(1H)-one; 4-amino-3-(5-morpholin-4-yl-1H-benzimidazol-2-30 yl)-5-[(pyridin-4-ylmethyl)oxy]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2yl)-5-(methyloxy)quinolin-2(1H)-one; 4-amino-3-(5-methyl-1H-benzimidazol-2-yl)-

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5-(methyloxy)quinolin-2(1H)-one; 4-amino-3-{5-[(2R,6S)-2,6-dimethylmorpholin-4yl]-1H-benzimidazol-2-yl}-5-(methyloxy)quinolin-2(1H)-one; 4-amino-3-(1Hbenzimidazol-2-yl)-5-morpholin-4-ylquinolin-2(1H)-one; 4-amino-3-(1Hbenzimidazol-2-yl)-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]quinolin-2(1H)-one; 4-5 amino-3-(1H-benzimidazol-2-yl)-5-(4-methylpiperazin-1-yl)quinolin-2(1H)-one; 4amino-5,6-dichloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one: 3-{5-[(2-morpholin-4-ylethyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4amino-3-{5-[(3-pyrrolidin-1-ylpropyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)one; 4-amino-3-{5-[(3-morpholin-4-ylpropyl)oxy]-1H-benzimidazol-2-yl}quinolin-10 2(1H)-one; 4-amino-6-fluoro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2yl}-6-fluoroquinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6fluoroquinolin-2(1H)-one; 4-amino-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-{5-[(tetrahydrofuran-2-ylmethyl)oxy]-1H-15 benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-6-fluoro-3-(6-fluoro-5-morpholin-4yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[6-fluoro-5-(4methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(5-{[2-(methyloxy)ethyl]oxy}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[4,6difluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-20 amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}-5fluoroquinolin-2(1H)-one; 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1Hbenzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-5-chloro-3-[5-(4-methylpiperazin-1yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one: 25 4-amino-5-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2yl}quinolin-2(1H)-one; 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-5-[(2R,6S)-2,6dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4amino-3-(6-thiomorpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-30 3-[5-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-

amino-3-{6-[3-(diethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-

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one; 4-amino-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-[5-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one; 4-amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazole-5-carboxamide; 4-amino-3-(5-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl)quinolin-2(1H)-amino-2-yl)quinolin-2-yl

benzimidazol-2-yl]-6-nitroquinolin-2(1H)-one; 4-amino-3-[5-(1,4'-bipiperidin-1'-ylcarbonyl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(4-

methylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[5-(1-oxidothiomorpholin-4-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 3-{5-[(4-acetylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl}-4-aminoquinolin-2(1H)-one; 4-amino-3-(5-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-(5-{[(3S)-3-

- (dimethylamino)pyrrolidin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-(5-{[4-(dimethylamino)piperidin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; methyl 2-(4-amino-5-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylate; 4-amino-3-[5-(1,3'-bipyrrolidin-1'-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-[5-(pyridin-3-yloxy)-1H-
- benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-5,6-bis(methyloxy)-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-[2-(dimethylamino)ethyl]-N-methyl-1H-benzimidazole-5-carboxamide; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-methyl-N-(1-methylpyrrolidin-3-yl)-1H-benzimidazole-5-carboxamide; 4-amino-3-{5-[(5-methyl-
- 2,5-diazabicyclo[2.2.1]hept-2-yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(4-cyclohexylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(2-piperidin-1-ylethyl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; ethyl 4-{[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-5-yl]amino}piperidine-1-carboxylate; 4-amino-3-[5-({(5R)-5-[(methyloxy)methyl]pyrrolidin-3-yl}amino)-1H-benzimidazol-3-yl}amino-1-yl}amino-1-yl
- amino-3-[5-({(5R)-5-[(methyloxy)methyl]pyrrolidin-3-yl}amino)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(pyridin-2-ylmethyl)amino]-1H-

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benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[5-(piperidin-3-ylamino)-1Hbenzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-5-fluoro-3-{5-[(pyridin-2ylmethyl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; ethyl 4-{[2-(4-amino-5fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-5-yl]amino}piperidine-1-5 carboxylate; 4-amino-5-fluoro-3-[5-(piperidin-3-ylamino)-1H-benzimidazol-2yl]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-bromoquinolin-2(1H)one; 4-amino-3-(1H-benzimidazol-2-yl)-7-bromoquinolin-2(1H)-one; 4-amino-3-(5bromo-1H-benzimidazol-2-yl)quinolin-2(1H)-one; N,N-dimethyl-2-(2-oxo-1,2dihydroquinolin-3-yl)-1H-benzimidazole-5-carboxamide; 4-amino-3-(5-thien-2-yl-10 1H-benzimidazol-2-yl)quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3yl)-N,N-dimethyl-1H-benzimidazole-5-sulfonamide; 4-amino-6-iodo-3-[5-(4methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(5-{2-[(dimethylamino)methyl]morpholin-4-yl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-chloro-6-15 iodoquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-nitroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-6-methylquinolin-2(1H)-one; 4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-difluoroquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-20 chloroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-bromoquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydroquinoline-6-carbonitrile; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoroquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-25 6,7-bis(methyloxy)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-dichloroquinolin-2(1H)-one; 1-[4-[(3S)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2dihydroquinolin-7-yl]piperidine-4-carboxamide; 4-[(3S)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(3-hydroxypropyl)amino]quinolin-30 2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(dimethylamino)-6-fluoroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-

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ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoroquinolin-2(1H)-one; 4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(4nitrophenyl)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-7-{[2-(dimethylamino)ethyl]amino}-6-fluoroquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(1Himidazol-1-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-[4-(methyloxy)phenyl]quinolin-2(1H)-one; 4-[(3S)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-morpholin-4ylquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6,7-difluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-10 3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(3-nitrophenyl)quinolin-2(1H)-one; 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-3-carboxamide; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-methylquinolin-2(1H)-one; 6-(3acetylphenyl)-4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-15 b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-chloroquinolin-2(1H)-one; 4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-6-fluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)-7morpholin-4-ylquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-20 (1H-benzimidazol-2-yl)-7-(cyclopropylamino)-6-fluoroquinolin-2(1H)-one; N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide; 4-[(3S)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(4-methylpiperazin-1-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-fluoro-7-(1H-imidazol-1-25 yl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3S)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(2-pyridin-2ylethyl)amino]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-piperidin-1-ylquinolin-2(1H)-one; 6-chloro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; ethyl 1-[4-[(3S)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-

dihydroquinolin-7-yl]piperidine-4-carboxylate; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-

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vlaminol-3-(1H-benzimidazol-2-yl)-6-(1-benzothien-2-yl)quinolin-2(1H)-one: 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7pyrrolidin-1-ylquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(trifluoromethyl)phenyl]quinolin-2(1H)-one; 5 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one; ethyl 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7yl]piperidine-3-carboxylate; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-(4-ethylphenyl)quinolin-2(1H)-one; 4-[(3S)-1-10 azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(2methylpropyl)amino]quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-5-methylquinolin-2(1H)-one; 4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-6-(2,4-dichlorophenyl)-3-(3H-imidazo[4,5b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-15 (1H-benzimidazol-2-yl)-6-[3-(trifluoromethyl)phenyl]quinolin-2(1H)-one; 3-(1Hbenzimidazol-2-yl)-4-(dimethylamino)quinolin-2(1H)-one; 4-hydroxy-3-(1Himidazo[4,5-f]quinolin-2-yl)quinolin-2(1H)-one; 4-hydroxy-3-(1H-imidazo[4,5b]pyridin-2-yl)quinolin-2(1H)-one; 4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid; 4-[4-20 [(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzamide; N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6yl]phenyl}acetamide; 3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid; 4-[4-25 [(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid; N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-7-fluoro-2-oxo-1,2-dihydroquinolin-6yl]phenyl}acetamide; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-7-chloro-6-(2-methylphenyl)quinolin-2(1H)-one; 4-[(3R)-1-30 azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2dihydroquinoline-7-carbonitrile; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-

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benzimidazol-2-yl)-7-(methyloxy)quinolin-2(1H)-one; 4-[4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2dihydroquinolin-7-yl]benzamide; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-fluoro-7-(methyloxy)quinolin-2(1H)-one; 4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloro-7-5 (dimethylamino)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(dimethylamino)-6-iodoquinolin-2(1H)-one; 3-[4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(1H-imidazol-1-yl)-2oxo-1,2-dihydroquinolin-6-yl]benzoic acid; 4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-7-piperidin-1-yl-1,2-dihydroquinolin-6-10 yl]benzoic acid; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazo1-2yl)-7-(methyloxy)-6-[4-(methylsulfonyl)phenyl]quinolin-2(1H)-one; 4-[(3R)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-8-methylquinolin-2(1H)one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7difluoroquinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6-methyl-4-(piperidin-3-15 ylamino)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one; 4-[(3S)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[3-(methyloxy)phenyl]quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-20 (piperidin-4-ylamino)quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-(pyrrolidin-3-ylamino)quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6-chloro-4-[(3morpholin-4-ylpropyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1Hbenzimidazol-2-yl)-4-(piperidin-4-ylamino)quinolin-2(1H)-one; 6-chloro-3-(5morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1Hbenzimidazol-2-yl)-4-(piperidin-3-ylamino)quinolin-2(1H)-one; 6-chloro-4-{[2-(dimethylamino)ethyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-chloro-3-(5-morpholin-4yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-

benzimidazol-2-yl)-4-[(piperidin-3-ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-3-

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(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-4-ylmethyl)aminolquinolin-2(1H)-one; 4-{[(1R,2R)-2-aminocyclohexyl]amino}-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-[(4-aminocyclohexyl)amino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-{[(2S)-2-amino-3-5 methylbutyl]amino}-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-({[4-(aminomethyl)phenyl]methyl}amino)-6-chloro-3-(5-morpholin-4yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1Hbenzimidazol-2-yl)-4-[(pyrrolidin-2-ylmethyl)amino]quinolin-2(1H)-one; 4-{[(1R)-1-(aminomethyl)propyllamino}-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2yl)quinolin-2(1H)-one; 4-{[(1S)-2-amino-1-(phenylmethyl)ethyl]amino}-6-chloro-3-10 (5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-4-{[3-(4methylpiperazin-1-yl)propyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-{[1-(phenylmethyl)piperidin-4-yl]amino}quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-15 4-yl-1H-benzimidazol-2-yl)-4-[(3-morpholin-4-ylpropyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-piperidin-1ylethyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(pyridin-3-ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-4-{[3-(1Himidazol-1-yl)propyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-20 2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(pyridin-4ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-4-{[2-(methylamino)ethyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-4-{[(2methyl-1-piperidin-4-yl-1H-benzimidazol-5-yl)methyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-25 benzimidazol-2-yl)-4-[(2-pyrrolidin-1-ylethyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(pyrrolidin-3-ylamino)quinolin-2(1H)one; 4-{[(1R,2R)-2-aminocyclohexyl]amino}-6-chloro-3-[5-(4-methylpiperazin-1yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-[(4-aminocyclohexyl)amino]-6chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-30 ({[4-(aminomethyl)phenyl]methyl}amino)-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 6-chloro-4-{[2-

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(methylamino)ethyl]amino}-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2yl]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2yl]-4-{[3-(4-methylpiperazin-1-yl)propyl]amino}quinolin-2(1H)-one; 6-chloro-3-[5- $(4-methylpiperazin-1-yl)-1 H-benzimidazol-2-yl]-4-\{[1-(phenylmethyl)piperidin-4-(phenylmethyl)$ yl]amino}quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1Hbenzimidazol-2-yl]-4-[(2-pyrrolidin-1-ylethyl)amino]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-(pyrrolidin-3ylamino)quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1Hbenzimidazol-2-yl]-4-(piperidin-4-ylamino)quinolin-2(1H)-one; 6-chloro-3-(5-10 morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-piperidin-2-ylethyl)amino]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-7-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 7-chloro-3-(5-morpholin-4-yl-1Hbenzimidazol-2-yl)-4-(piperidin-3-ylamino)quinolin-2(1H)-one; 6-chloro-3-[5-(4methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-15 benzimidazol-2-yl]-4-{[(2S)-pyrrolidin-2-ylmethyl]amino}quinolin-2(1H)-one; 6 $chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-\{[(2R)-pyrrolidin-2-yl]-4-\{(2R)-pyrrolidin-2-yl)-1H-benzimidazol-2-yl]-4-yl]$ ylmethyl]amino}quinolin-2(1H)-one; 6-chloro-4-({[(2S)-1-ethylpyrrolidin-2 $yl] methyl \} amino) - 3 - [5 - (4 - methylpiperazin - 1 - yl) - 1 H - benzimidazol - 2 - yl] quinolin-line (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl) - 1 H - benzimidazol - 2 - yl] quinoline (1 - yl)$ 2(1H)-one; 6-chloro-4-({[(2R)-1-ethylpyrrolidin-2-yl]methyl}amino)-3-[5-(4-20 methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-[(3S)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[4-(methyloxy)phenyl]quinolin-2(1H)-one; and 6-(3-aminophenyl)-4-[(3S)-1azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one.

Each of the above compounds displayed an IC₅₀ value of less than 10 μM with respect to VEGFR1, VEGFR2, and bFGF.

It should be understood that the organic compounds according to the invention may exhibit the phenomenon of tautomerism. As the chemical structures within this specification can only represent one of the possible tautomeric forms, it

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should be understood that the invention encompasses any tautomeric form of the drawn structure.

It is understood that the invention is not limited to the embodiments set forth herein for illustration, but embraces all such forms thereof as come within the scope of the following claims.

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CLAIMS

What is claimed is:

- 1 1. A compound having the structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a
- 3 pharmaceutically acceptable salt of the tautomer

$$R^{2}$$
 R^{3}
 R^{4}
 R^{9}
 R^{9}

I

5 wherein,

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Y is selected from the group consisting of -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, substituted and unsubstituted alkynyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted heterocyclyloxyalkyl groups, substituted and unsubstituted hydroxyalkyl groups, and substituted and unsubstituted aryloxyalkyl groups;

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19	Z is selected from the group consisting of O, S, and NR ¹⁴ groups;
20	R ¹ , R ² , R ³ , and R ⁴ may be the same or different and are
21	independently selected from the group consisting of H, Cl, Br, F, I,
22	-CN, -NO ₂ , -OH, -OR ¹⁵ groups, -NR ¹⁶ R ¹⁷ groups, substituted and
23	unsubstituted amidinyl groups, substituted and unsubstituted
24	guanidinyl groups, substituted and unsubstituted primary, secondary,
25	and tertiary alkyl groups, substituted and unsubstituted aryl groups,
26	substituted and unsubstituted alkenyl groups, substituted and
27	unsubstituted alkynyl groups, substituted and unsubstituted
- <i>.</i> 28	heterocyclyl groups, substituted and unsubstituted aminoalkyl groups
29	substituted and unsubstituted alkylaminoalkyl groups, substituted and
30	unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted
31	arylaminoalkyl groups, substituted and unsubstituted
32 \	diarylaminoalkyl groups, substituted and unsubstituted
33	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
34	heterocyclylalkyl groups, substituted and unsubstituted
35	diheterocyclylaminoalkyl groups, substituted and unsubstituted
36	(heterocyclyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
37	(heterocyclyl)(aryl)aminoalkyl groups, and -C(=O)R ¹⁸ groups;
	(
38	R ⁵ , R ⁶ , R ⁷ , and R ⁸ may be the same or different and are
19	independently selected from the group consisting of H, Cl, Br, F, I,
Ю	-NO ₂ , -OH, -OR ¹⁹ groups, -NR ²⁰ R ²¹ groups, -SH, -SR ²² groups,
1	-S(=O)R ²³ groups, -S(=O) ₂ R ²⁴ groups, -CN, substituted and
12	unsubstituted amidinyl groups, substituted and unsubstituted
3	guanidinyl groups, substituted and unsubstituted primary, secondary,
4	and tertiary alkyl groups, substituted and unsubstituted aryl groups,
5	substituted and unsubstituted alkenyl groups, substituted and
6	unsubstituted alkynyl groups, substituted and unsubstituted
7	heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl
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48	groups, -C(=O)R ²⁵ groups, substituted and unsubstituted aminoalkyl
49	groups, substituted and unsubstituted alkylaminoalkyl groups,
50	substituted and unsubstituted dialkylaminoalkyl groups, substituted
51	and unsubstituted arylaminoalkyl groups, substituted and
52	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
53	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
54	heterocyclylaminoalkyl groups, substituted and unsubstituted
55	diheterocyclylaminoalkyl groups, substituted and unsubstituted
56	(heterocyclyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
57	(heterocyclyl)(aryl)aminoalkyl groups, substituted and unsubstituted
58	hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl
59	groups, substituted and unsubstituted aryloxyalkyl groups, and
60	substituted and unsubstituted heterocyclyloxyalkyl groups;
61	R ⁹ and R ¹⁴ may be the same or different and are independently
62	selected from the group consisting of H, -OH, substituted and
63	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy
64	groups, -NH2, substituted and unsubstituted alkylamino groups,
65	substituted and unsubstituted arylamino groups, substituted and
66	unsubstituted dialkylamino groups, substituted and unsubstituted
67	diarylamino groups, substituted and unsubstituted (alkyl)(aryl)amino
68	groups, substituted and unsubstituted alkyl groups, substituted and
69	unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, and
70	-C(=O)-aryl groups;
71	R ¹⁰ is selected from the group consisting of substituted and
72	unsubstituted aryl groups, substituted and unsubstituted heterocyclyl
73	groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups,
74	-C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH ₂ ,
75	-C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,
76	-C(=O)N(alkyl) ₂ groups, -C(=O)N(aryl) ₂ groups,

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11	-C(=O)N(alkyl)(aryl) groups, -NH2, -NH(alkyl) groups, -NH(aryl)
78	groups, -N(alkyl)2 groups, -N(alkyl)(aryl) groups, -N(aryl)2 groups,
79	-NH(heterocyclyl) groups, -N(heterocyclyl)2 groups,
80	-N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl),
81	-C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl) ₂ groups,
82	-C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl)
83	groups, and substituted and unsubstituted heterocyclylalkyl groups;
84	R ¹¹ is selected from the group consisting of H, -NH ₂ , -NH(alkyl)
85	groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(aryl)2 groups,
86	-N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)2
87	groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl)
88	groups, -O-alkyl groups, O-aryl groups, heterocyclyloxyalkyl
89	groups, and substituted and unsubstituted aryl groups;
90	R ¹² is selected from the group consisting of H, substituted and
91	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
92	and substituted and unsubstituted heterocyclyl groups;
93	R ¹³ is selected from the group consisting of substituted and
94	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
95	substituted and unsubstituted heterocyclyl groups, -OH, alkoxy
96	groups, aryloxy groups, -NH2, substituted and unsubstituted
97	heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl
98	groups, substituted and unsubstituted alkylaminoalkyl groups,
99	substituted and unsubstituted dialkylaminoalkyl groups, substituted
100	and unsubstituted arylaminoalkyl groups, substituted and
101	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
102	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
103	alkylamino groups, substituted and unsubstituted arylamino groups,
104	substituted and unsubstituted dialkylamino groups, substituted and

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105	unsubstituted diarylamino groups, substituted and unsubstituted
106	(alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups,
. 107	-C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups,
108	-C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,
109	-C(=O)N(alkyl) ₂ groups, -C(=O)N(aryl) ₂ groups,
110	-C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups,
111	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,
112	-C(=O)-N(heterocyclyl) ₂ groups, -C(=O)N(aryl)(heterocyclyl)
113	groups, substituted and unsubstituted heterocyclylaminoalkyl groups,
114	substituted and unsubstituted hydroxyalkyl groups, substituted and
115	unsubstituted alkoxyalkyl groups, substituted and unsubstituted
116	aryloxyalkyl groups, substituted and unsubstituted
. 117	heterocyclyloxyalkyl groups, and -C(=O)-N(alkyl)(heterocyclyl)
118	groups;
119	R ¹⁵ and R ¹⁹ may be the same or different and are independently
120	selected from the group consisting of substituted and unsubstituted
121	alkyl groups, substituted and unsubstituted aryl groups, substituted
122	and unsubstituted heterocyclyl groups, substituted and unsubstituted
123	heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups,
124	-C(=O)-aryl groups, -C(=O)NH ₂ , -C(=O)NH(alkyl) groups,
125	-C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2
126	groups, -C(=O)N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,
127	-N(heterocyclyl)2 groups, -N(alkyl)(heterocyclyl) groups,
128	-N(aryl)(heterocyclyl) groups, substituted and unsubstituted
129	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl
130	groups, substituted and unsubstituted dialkylaminoalkyl groups,
131	substituted and unsubstituted arylaminoalkyl groups, substituted and
132	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
133	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
134	heterocyclylaminoalkyl, substituted and unsubstituted

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135	diheterocyclylaminoalkyl, substituted and unsubstituted
136	(heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted
137	(heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted
138	alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl
139	groups, substituted and unsubstituted aryloxyalkyl groups, and
140	substituted and unsubstituted heterocyclyloxyalkyl groups;
141	R^{16} and R^{20} may be the same or different and are independently
142	selected from the group consisting of H, substituted and unsubstituted
143	alkyl groups, substituted and unsubstituted aryl groups, and
144	substituted and unsubstituted heterocyclyl groups;
145	R ¹⁷ and R ²¹ may be the same or different and are independently
146	selected from the group consisting of H, substituted and unsubstituted
147	alkyl groups, substituted and unsubstituted aryl groups, substituted
148	and unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl
149	groups, $-C(=O)$ -aryl groups, $-C(=O)NH_2$, $-C(=O)NH(alkyl)$
150	groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups,
151	-C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups,
152	-C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and
153	unsubstituted heterocyclylalkyl groups, substituted and unsubstituted
154	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl
155	groups, substituted and unsubstituted dialkylaminoalkyl groups,
156	substituted and unsubstituted arylaminoalkyl groups, substituted and
157	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
158	(alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,
159	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,
160	-C(=O)N(heterocyclyl) ₂ groups, -C(=O)N(aryl)(heterocyclyl)
161	groups, substituted and unsubstituted heterocyclylaminoalkyl groups,
162	substituted and unsubstituted diheterocyclylaminoalkyl groups,
163	substituted and unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups.

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164	substituted and unsubstituted (heterocyclyl)(aryl)aminoalkyl groups
165	substituted and unsubstituted hydroxyalkyl groups, substituted and
166	unsubstituted alkoxyalkyl groups, substituted and unsubstituted
167	aryloxyalkyl groups, substituted and unsubstituted
168	heterocyclyloxyalkyl groups, and $-C(=O)-N(alkyl)(heterocyclyl)$
169	groups;
170	R^{18} , R^{23} , R^{24} , and R^{25} may be the same or different and are
171	independently selected from the group consisting of H, -NH ₂ ,
172	-NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(aryl)2
173	groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,
174	-N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,
175	-N(heterocyclyl)2 groups, substituted and unsubstituted alkyl groups
. 176	substituted and unsubstituted aryl groups, -OH, substituted and
177	unsubstituted alkoxy groups, substituted and unsubstituted
178	heterocyclyl groups, substituted and unsubstituted aryloxy groups,
179	heterocyclyloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH
180	groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups,
181	-N(alkyl)O-aryl groups, and -N(aryl)O-aryl groups; and
182	R ²² is selected from the group consisting of substituted and
183	unsubstituted alkyl groups, substituted and unsubstituted aryl groups
184	and substituted and unsubstituted heterocyclyl groups.
1	2. The compound according to claim 1, wherein Y is selected
2	from the group consisting of $-OR^{10}$ groups, $-NR^{12}R^{13}$ groups, and substituted and
3	unsubstituted alkynyl groups.
1	3. The compound according to claim 1, wherein Z is an -NR ¹⁴
2	group.

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- 1 4. The compound according to claim 1, wherein R¹ is selected
- 2 from the group consisting of -H, substituted and unsubstituted alkoxy groups,
- 3 substituted and unsubstituted heterocyclylalkoxy groups, substituted and
- 4 unsubstituted heterocyclyloxy groups, and substituted and unsubstituted heterocyclyl
- 5 groups.
- 1 5. The compound according to claim 1, wherein R² is selected
- 2 from the group consisting of H, F, Cl, -NO2, substituted and unsubstituted
- 3 heterocyclylalkoxy groups, and substituted and unsubstituted heterocyclyl groups.
- 1 6. The compound according to claim 1, wherein R^6 or R^7 is an
- 2 alkyl group.
- The compound according to claim 1, wherein R^6 or R^7 is an
- 2 -OR¹⁹ group and R¹⁹ is an alkyl group, an aryl group, a heterocyclyl group, or a
- 3 heterocyclylalkyl group.
- 1 8. A compound having the structure I, a tautomer of the
- 2 compound, a pharmaceutically acceptable salt of the compound, or a
- 3 pharmaceutically acceptable salt of the tautomer

$$R^3$$
 R^4
 R^8
 R^8

4

I

5 wherein,

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U	I is selected from the group consisting of $-OR^{10}$ groups, $-C(=O)-R^{10}$
7	groups, -NR ¹² R ¹³ groups, substituted and unsubstituted alkynyl
8	groups, substituted and unsubstituted heterocyclylalkyl groups,
9	substituted and unsubstituted alkylaminoalkyl groups, substituted and
10	unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted
11	arylaminoalkyl groups, substituted and unsubstituted
12	diarylaminoalkyl groups, substituted and unsubstituted
13	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
14	heterocyclylaminoalkyl groups, substituted and unsubstituted
15	saturated heterocyclyl groups, substituted and unsubstituted
16	heterocyclyloxyalkyl groups, substituted and unsubstituted
17	hydroxyalkyl groups, and substituted and unsubstituted aryloxyalkyl
18	groups;
19	Z is selected from the group consisting of O, S, and NR ¹⁴ groups;
20	R^1 , R^2 , R^3 , and R^4 may be the same or different and are
21	independently selected from the group consisting of H, Cl, Br, F, I,
22 .	-CN, -NO ₂ , -OH, -OR ¹⁵ groups, -NR ¹⁶ R ¹⁷ groups, substituted and
23	unsubstituted amidinyl groups, substituted and unsubstituted
24	guanidinyl groups, substituted and unsubstituted primary, secondary,
25	and tertiary alkyl groups, substituted and unsubstituted aryl groups,
26	substituted and unsubstituted alkenyl groups, substituted and
27	unsubstituted alkynyl groups, substituted and unsubstituted
28	heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,
29	substituted and unsubstituted alkylaminoalkyl groups, substituted and
30	unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted
31	arylaminoalkyl groups, substituted and unsubstituted
32	diarylaminoalkyl groups, substituted and unsubstituted
33	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
34	heterocyclylalkyl groups; and $-C(=O)R^{18}$ groups:

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R ⁵ , R ⁶ , R ⁷ , and R ⁸ may be the same or different and are
independently selected from the group consisting of H, Cl, Br, F, I,
-NO ₂ , -OH, -OR ¹⁹ groups, -NR ²⁰ R ²¹ groups, -SH, -SR ²² groups,
-S(=O)R ²³ groups, -S(=O) ₂ R ²⁴ groups, -CN, substituted and
unsubstituted amidinyl groups, substituted and unsubstituted
guanidinyl groups, substituted and unsubstituted primary, secondary
and tertiary alkyl groups, substituted and unsubstituted aryl groups,
substituted and unsubstituted alkenyl groups, substituted and
unsubstituted alkynyl groups, substituted and unsubstituted
heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl
groups, -C(=O)R ²⁵ groups, substituted and unsubstituted aminoalkyl
groups, substituted and unsubstituted alkylaminoalkyl groups,
substituted and unsubstituted dialkylaminoalkyl groups, substituted
and unsubstituted arylaminoalkyl groups, substituted and
unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
heterocyclylaminoalkyl groups, substituted and unsubstituted
hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl
groups, substituted and unsubstituted aryloxyalkyl groups, and
substituted and unsubstituted heterocyclyloxyalkyl groups;
R9 is selected from the group consisting of -OH, substituted and
unsubstituted alkoxy groups, substituted and unsubstituted aryloxy
groups, -NH2, substituted and unsubstituted alkylamino groups,
substituted and unsubstituted arylamino groups, substituted and
unsubstituted dialkylamino groups, substituted and unsubstituted
diarylamino groups, substituted and unsubstituted (alkyl)(aryl)amino
groups, substituted and unsubstituted alkyl groups, substituted and
unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, and
-C(=O)-aryl groups;

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04	R'' is selected from the group consisting of substituted and
65	unsubstituted aryl groups, substituted and unsubstituted heterocycly
66	groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups,
67	-C(=0)O-alkyl groups, -C(=0)O-aryl groups, -C(=0)NH ₂ ,
68	-C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,
69	$-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups,
70	-C(=O)N(alkyl)(aryl) groups, -NH2, -NH(alkyl) groups, -NH(aryl)
71	groups, -N(alkyl)2 groups, -N(alkyl)(aryl) groups, -N(aryl)2 groups,
72	-C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)2 groups,
73	-C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl)
74	groups, and substituted and unsubstituted heterocyclylalkyl groups;
75	R ¹¹ is selected from the group consisting of H, -NH ₂ , -NH(alkyl)
76	groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(aryl)2 groups,
77	-N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)2
78	groups, -N(alkyl)(heterocyclyl) groups, -O-alkyl groups, O-aryl
79	groups, substituted and unsubstituted alkyl groups, and substituted
80	and unsubstituted aryl groups;
81	R ¹² is selected from the group consisting of H, substituted and
82	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
83	and substituted and unsubstituted heterocyclyl groups;
84	R ¹³ is selected from the group consisting of H, substituted and
85	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
86	substituted and unsubstituted heterocyclyl groups, -OH, alkoxy
87	groups, aryloxy groups, -NH2, substituted and unsubstituted
88	alkylamino groups, substituted and unsubstituted arylamino groups,
89	substituted and unsubstituted dialkylamino groups, substituted and
90	unsubstituted diarylamino groups, substituted and unsubstituted
91	(alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups,
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92	-C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups,
93	-C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,
94	-C(=O)N(alkyl) ₂ groups, -C(=O)N(aryl) ₂ groups,
95	-C(=O)N(alkyl)(aryl) groups, substituted and unsubstituted
96	heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl
97	groups, substituted and unsubstituted alkylaminoalkyl groups,
98	substituted and unsubstituted dialkylaminoalkyl groups, substituted
99	and unsubstituted arylaminoalkyl groups, substituted and
100	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
101	(alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,
102	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,
103	-C(=O)-N(heterocyclyl) ₂ groups, -C(=O)N(aryl)(heterocyclyl)
104	groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and
105	unsubstituted heterocyclylaminoalkyl groups, substituted and
106	unsubstituted hydroxyalkyl groups, substituted and unsubstituted
107	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl
108	groups, and substituted and unsubstituted heterocyclyloxyalkyl
109	groups;
110	R ¹⁴ is selected from the group consisting of H, -OH, substituted and
111	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy
112	groups, -NH2, substituted and unsubstituted alkylamino groups,
113	substituted and unsubstituted arylamino groups, substituted and
114	unsubstituted dialkylamino groups, substituted and unsubstituted
115	diarylamino groups, substituted and unsubstituted (alkyl)(aryl)amino
116	groups, substituted and unsubstituted alkyl groups, substituted and
117	unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, and
118	-C(=O)-aryl groups;
119	R ¹⁵ and R ¹⁹ may be the same or different and are independently
120	selected from the group consisting of substituted and unsubstituted

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121	alkyl groups, substituted and unsubstituted aryl groups, substituted
122	and unsubstituted heterocyclyl groups, substituted and unsubstituted
123	heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups,
124	$-C(=O)$ -aryl groups, $-C(=O)NH_2$, $-C(=O)NH(alkyl)$ groups,
125	-C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2
126	groups, -C(=O)N(alkyl)(aryl) groups, substituted and unsubstituted
127	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl
128	groups, substituted and unsubstituted dialkylaminoalkyl groups,
129	substituted and unsubstituted arylaminoalkyl groups, substituted and
130	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
131	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
132	heterocyclylaminoalkyl, substituted and unsubstituted
133	diheterocyclylaminoalkyl, substituted and unsubstituted
134	(heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted
135	(heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted
136	alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl
137	groups, substituted and unsubstituted aryloxyalkyl groups, and
138	substituted and unsubstituted heterocyclyloxyalkyl groups;
139	R^{16} and R^{20} may be the same or different and are independently
140	selected from the group consisting of H, substituted and unsubstituted
141	alkyl groups, substituted and unsubstituted aryl groups, and
142	substituted and unsubstituted heterocyclyl groups;
143	R ¹⁷ and R ²¹ may be the same or different and are independently
144	selected from the group consisting of H, substituted and unsubstituted
145	alkyl groups, substituted and unsubstituted aryl groups, substituted
146	and unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl
147	groups, -C(=O)-aryl groups,-C(=O)NH ₂ , -C(=O)NH(alkyl)
148	groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl) ₂ groups,
149	-C(=O)N(aryl) ₂ groups, -C(=O)N(alkyl)(aryl) groups,

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150	-C(=O)O-alkyl groups, $-C(=O)O$ -aryl groups, substituted and
151	unsubstituted heterocyclylalkyl groups, substituted and unsubstituted
152	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl
153	groups, substituted and unsubstituted dialkylaminoalkyl groups,
154	substituted and unsubstituted arylaminoalkyl groups, substituted and
155	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
156	(alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,
157	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,
158	-C(=O)-N(heterocyclyl) ₂ groups, -C(=O)N(aryl)(heterocyclyl)
159	groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and
160	unsubstituted heterocyclylaminoalkyl groups, substituted and
161	unsubstituted hydroxyalkyl groups, substituted and unsubstituted
162	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl
163	groups, and substituted and unsubstituted heterocyclyloxyalkyl
164	groups;
165	R ¹⁸ , R ²³ , R ²⁴ , and R ²⁵ may be the same or different and are
166	independently selected from the group consisting of H, -NH ₂ ,
167	-NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(aryl)2
168	groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,
169	-N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,
170	-N(heterocyclyl)2 groups, substituted and unsubstituted alkyl groups,
171	substituted and unsubstituted aryl groups, -OH, substituted and
172	unsubstituted alkoxy groups, substituted and unsubstituted
173	heterocyclyl groups, substituted and unsubstituted aryloxy groups,
174	-NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl
175	groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and
176	-N(aryl)O-aryl groups; and

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177	R ²² is selected from the group consisting of substituted and		
178	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,		
179	and substituted and unsubstituted heterocyclyl groups.		
1	9. The compound according to claim 8, wherein Y is se	lected	
. 2	from the group consisting of -OR10 groups, -NR12R13 groups, and substitute	ed and	
3			
1	10	14	
2	10. The compound according to claim 8, wherein Z is an	-NR ¹⁴	
2	group.		
1	11. The compound according to claim 8, wherein R ¹ is se	lected	
2	from the group consisting of -H, substituted and unsubstituted alkoxy group	os,	
3	substituted and unsubstituted heterocyclylalkoxy groups, substituted and		
4	unsubstituted heterocyclyloxy groups, and substituted and unsubstituted hete	erocyclyl	
5	groups.		
1	12. The compound according to claim 8, wherein R ² is se	lected	
2	from the group consisting of H, F, Cl, -NO2, substituted and unsubstituted		
3	heterocyclyl groups, and substituted and unsubstituted heterocyclylalkoxy gr	oups.	
-			
1	13. The compound according to claim 8, wherein R ⁶ or R ⁷	' is an	
2	alkyl group.		
1	14. The compound according to claim 8, wherein R ⁶ or R ⁷		
2	14. The compound according to claim 8, wherein R ⁶ or R ⁷ -OR ¹⁹ group and R ¹⁹ is an alkyl group, an aryl group, a heterocyclyl group,		
3	heterocyclylalkyl group.	or a	
3	neterocycrytaikyr group.		

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1 15. A compound having the structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer

$$R^2$$
 R^3
 R^4
 R^9

I

6 wherein,

Y is selected from the group consisting of -OH, SH, alkylthio groups, arylthio groups, -OR¹⁰ groups, -C(=O)-R¹¹ groups, -NR¹²R¹³ groups, -CN, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkynyl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted

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21	and unsubstituted hydroxyalkyl groups, substituted and unsubstituted
22	alkoxyalkyl groups, and substituted and unsubstituted aryloxyalkyl
23	groups;
24	Z is selected from the group consisting of O, S, and NR ¹⁴ groups;
25	R ¹ , R ² , R ³ , and R ⁴ may be the same or different and are
26	independently selected from the group consisting of H, Cl, Br, F, I,
27	-CN, -NO ₂ , -OH, -OR ¹⁵ groups, -NR ¹⁶ R ¹⁷ groups, substituted and
28	unsubstituted amidinyl groups, substituted and unsubstituted
29	guanidinyl groups, substituted and unsubstituted primary, secondary,
30	and tertiary alkyl groups, substituted and unsubstituted aryl groups,
31	substituted and unsubstituted alkenyl groups, substituted and
32	unsubstituted alkynyl groups, substituted and unsubstituted
33	heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,
34	substituted and unsubstituted alkylaminoalkyl groups, substituted and
35	unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted
36	arylaminoalkyl groups, substituted and unsubstituted
37	diarylaminoalkyl groups, substituted and unsubstituted
38	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
39	heterocyclylalkyl groups, and $-C(=O)R^{18}$ groups;
40	R ⁵ , R ⁶ , R ⁷ , and R ⁸ may be the same or different and are
41	independently selected from the group consisting of H, Cl, Br, F, I,
42	-NO ₂ , -OH, -OR ¹⁹ groups, -NR ²⁰ R ²¹ groups, -SH, -SR ²² groups,
43	-S(=O)R ²³ groups, -S(=O) ₂ R ²⁴ groups, -CN, substituted and
44	unsubstituted amidinyl groups, substituted and unsubstituted
45	guanidinyl groups, substituted and unsubstituted primary, secondary,
46	and tertiary alkyl groups, substituted and unsubstituted aryl groups,
47	substituted and unsubstituted alkenyl groups, substituted and
48	unsubstituted alkynyl groups, substituted and unsubstituted

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.49	heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl
50	groups, substituted and unsubstituted dialkylaminoalkyl groups,
51	substituted and unsubstituted arylaminoalkyl groups, substituted and
52	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
53	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
54	heterocyclylalkyl groups, -C(=O)R ²⁵ groups, substituted and
55	unsubstituted aminoalkyl groups, substituted and unsubstituted
56	heterocyclylaminoalkyl groups, substituted and unsubstituted
57	hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl
58	groups, substituted and unsubstituted aryloxyalkyl groups, and
59	substituted and unsubstituted heterocyclyloxyalkyl groups;
60	R ⁹ and R ¹⁴ may be the same or different and are independently
61	selected from the group consisting of H, -OH, substituted and
62	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy
63	groups, -NH2, substituted and unsubstituted alkylamino groups,
64	substituted and unsubstituted arylamino groups, substituted and
65	unsubstituted dialkylamino groups, substituted and unsubstituted
66	diarylamino groups, substituted and unsubstituted (alkyl)(aryl)amino
67	groups, substituted and unsubstituted alkyl groups, substituted and
68	unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, and
69	-C(=O)-aryl groups;
70	R ¹⁰ is selected from the group consisting of substituted and
71	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
72	substituted and unsubstituted heterocyclyl groups, substituted and
73	unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl
74	groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl
75	groups, -C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)
76	groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups,
77	-C(=O)N(alkyl)(aryl) groups, -NH2, -NH(alkyl) groups, -NH(aryl)

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78	groups, -N(alkyl)2 groups, -N(alkyl)(aryl) groups, -N(aryl)2 groups,
79	-C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl) ₂ groups,
80	-C(=O)N(alkyl)(heterocyclyl) groups, and
81	-C(=O)N(aryl)(heterocyclyl) groups;
82	R ¹¹ is selected from the group consisting of H, -OH, alkoxy groups,
83	aryloxy groups, -NH ₂ , -NH(alkyl) groups, -NH(aryl) groups,
84	-N(alkyl)2 groups, -N(aryl)2 groups, -N(alkyl)(aryl) groups,
85	substituted and unsubstituted alkyl groups, -NH(heterocyclyl) groups
86	-N(heterocyclyl) ₂ groups, -N(alkyl)(heterocyclyl) groups, and
87	substituted and unsubstituted aryl groups;
88	R ¹² is selected from the group consisting of H, substituted and
89	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
90	and substituted and unsubstituted heterocyclyl groups;
91	R ¹³ is selected from the group consisting of H, substituted and
92	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
93	substituted and unsubstituted heterocyclyl groups, -OH, alkoxy
94	groups, aryloxy groups, -NH ₂ , substituted and unsubstituted
95	heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl
96	groups, substituted and unsubstituted alkylaminoalkyl groups,
97	substituted and unsubstituted dialkylaminoalkyl groups, substituted
98	and unsubstituted arylaminoalkyl groups, substituted and
99	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
100	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
101	alkylamino groups, substituted and unsubstituted arylamino groups,
102	substituted and unsubstituted dialkylamino groups, substituted and
103	unsubstituted diarylamino groups, substituted and unsubstituted
104	(alkyl)(aryl)amino groups, -C(=0)H, -C(=0)-alkyl groups,
105	-C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups,

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106	-C(=O)NH2, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,
107	-C(=O)N(alkyl) ₂ groups, -C(=O)N(aryl) ₂ groups,
108	-C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups,
109	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,
110	-C(=O)-N(heterocyclyl) ₂ groups, -C(=O)-N(alkyl)(heterocyclyl)
111	groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and
112	unsubstituted heterocyclylaminoalkyl groups, substituted and
113	unsubstituted hydroxyalkyl groups, substituted and unsubstituted
114	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl
115	groups, and substituted and unsubstituted heterocyclyloxyalkyl
116	groups;
117	R ¹⁵ and R ¹⁹ may be the same or different and are independently
118	selected from the group consisting of substituted and unsubstituted
119	alkyl groups, substituted and unsubstituted aryl groups, substituted
120	and unsubstituted heterocyclyl groups, substituted and unsubstituted
121	heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups,
122	$C(=0)$ -aryl groups, - $C(=0)NH_2$, - $C(=0)NH(alkyl)$ groups,
123	-C(=0)NH(aryl) groups, -C(=0)N(alkyl) ₂ groups, -C(=0)N(aryl) ₂
124	groups, -C(=O)N(alkyl)(aryl) groups, substituted and unsubstituted
125	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl
126	groups, substituted and unsubstituted dialkylaminoalkyl groups,
127	substituted and unsubstituted arylaminoalkyl groups, substituted and
128	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
129	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
130	heterocyclylaminoalkyl, substituted and unsubstituted
131	diheterocyclylaminoalkyl, substituted and unsubstituted
132	(heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted
133	(heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted
134	alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl

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133	groups, substituted and unsubstituted aryloxyalkyl groups, and
136	substituted and unsubstituted heterocyclyloxyalkyl groups;
137	D16 and D20 b. 4b 1100
	R ¹⁶ and R ²⁰ may be the same or different and are independently
138	selected from the group consisting of H, substituted and unsubstituted
139	alkyl groups, substituted and unsubstituted aryl groups, and
140	substituted and unsubstituted heterocyclyl groups;
141	R ¹⁷ and R ²¹ may be the same or different and are independently
142	selected from the group consisting of H, substituted and unsubstituted
143	alkyl groups, substituted and unsubstituted aryl groups, substituted
144	and unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl
145	groups, -C(=O)-aryl groups, -C(=O)NH ₂ , -C(=O)NH(alkyl)
146	groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)2 groups,
147	-C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups,
148	-C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and
149	unsubstituted heterocyclylalkyl groups, substituted and unsubstituted
150	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl
151	groups, substituted and unsubstituted dialkylaminoalkyl groups,
152	substituted and unsubstituted arylaminoalkyl groups, substituted and
153	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
154	(alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,
155	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,
156	-C(=O)-N(heterocyclyl) ₂ groups, -C(=O)-N(alkyl)(heterocyclyl)
157	groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and
158	unsubstituted heterocyclylaminoalkyl groups, substituted and
159	unsubstituted hydroxyalkyl groups, substituted and unsubstituted
160	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl
161	groups, and substituted and unsubstituted heterocyclyloxyalkyl
162	groups;

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103	R', R', and R' may be the same or different and are
164	independently selected from the group consisting of H, -NH2,
165	-NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(aryl)2
166	groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,
167	-N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,
168	-N(heterocyclyl)2 groups, substituted and unsubstituted alkyl groups,
169	substituted and unsubstituted aryl groups, -OH, substituted and
170	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy
171	groups, substituted and unsubstituted heterocyclyl groups, -NHOH,
172	-N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups,
173	-N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and -N(aryl)O-aryl
174	groups; and
175	R ²² is selected from the group consisting of substituted and
176	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
177	and substituted and unsubstituted heterocyclyl groups;
178	and further wherein at least one of R ⁵ , R ⁶ , R ⁷ , or R ⁸ is selected from
179	the group consisting of substituted and unsubstituted amidinyl groups,
180	substituted and unsubstituted guanidinyl groups, substituted and
181	unsubstituted saturated heterocyclyl groups, substituted and
182	unsubstituted alkylaminoalkyl groups, substituted and unsubstituted
183	dialkylaminoalkyl groups, substituted and unsubstituted
184	arylaminoalkyl groups, substituted and unsubstituted
185	diarylaminoalkyl groups, substituted and unsubstituted
186	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
187	heterocyclylalkyl groups, substituted and unsubstituted
188	heterocyclylaminoalkyl groups, substituted and unsubstituted
189	hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl
190	groups, substituted and unsubstituted aryloxyalkyl groups, and
191	substituted and unsubstituted heterocyclyloxyalkyl groups; -OR ¹⁹

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192	groups wherein R ¹⁹ is selected from the group consisting of
193	substituted and unsubstituted aryl groups, substituted and
194	unsubstituted heterocyclyl groups, substituted and unsubstituted
195	heterocyclylalkyl groups, -C(=O)H, -C(=O)-aryl groups,
196	-C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,
197	$-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups,
198	-C(=O)N(alkyl)(aryl) groups, substituted and unsubstituted
199	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl
200	groups, substituted and unsubstituted dialkylaminoalkyl groups,
201	substituted and unsubstituted arylaminoalkyl groups, substituted and
202	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
203	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
204	heterocyclylaminoalkyl groups, substituted and unsubstituted
205	diheterocyclylaminoalkyl groups, substituted and unsubstituted
206	(heterocyclyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
207	(heterocyclyl)(aryl)aminoalkyl groups, substituted and unsubstituted
208	hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl
209	groups, substituted and unsubstituted aryloxyalkyl groups, and
210	substituted and unsubstituted heterocyclyloxyalkyl groups; -NR ²⁰ R ²¹
211	groups wherein R ²⁰ is selected from the group consisting of
212	substituted and unsubstituted heterocyclyl groups; -NR ²⁰ R ²¹ groups
213	wherein R ²¹ is selected from the group consisting of substituted and
214	unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-aryl groups,
215	-C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,
216	-C(=O)N(alkyl) ₂ groups, -C(=O)N(aryl) ₂ groups,
217	-C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups,
218	-C(=O)O-aryl groups, substituted and unsubstituted aminoalkyl
219	groups, substituted and unsubstituted alkylaminoalkyl groups,
220	substituted and unsubstituted dialkylaminoalkyl groups, substituted
221	and unsubstituted arylaminoalkyl groups, substituted and
222	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted

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223	3 (alkyl)(aryl)aminoalkyl groups, substituted and a	ınsubstituted
224	4 heterocyclylaminoalkyl groups, substituted and	unsubstituted
225	5 hydroxyalkyl groups, substituted and unsubstitut	ed alkoxyalkyl
226	6 groups, substituted and unsubstituted aryloxyalk	yl groups, substituted
227	and unsubstituted heterocyclylalkyl groups, and	substituted and
228	8 unsubstituted heterocyclyloxyalkyl groups; and	C(=O)R ²⁵ groups
229	9 wherein R ²⁵ is selected from the group consisting	g of H, -NH2,
230	O -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl):	groups, -N(aryl)2
231	groups, -N(alkyl)(aryl) groups, -NH(heterocycly	l) groups,
232	2 -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)	(aryl) groups,
233	3 -N(heterocyclyl) ₂ groups, substituted and unsubs	tituted aryl groups,
234	substituted and unsubstituted aryloxy groups, and substituted and	
235	unsubstituted heterocyclyl groups.	
1	16. The compound according to claim 15, wh	erein Y is selected
2	2 from the group consisting of -OR ¹⁰ groups, -NR ¹² R ¹³ groups, as	nd substituted and
3	3 unsubstituted alkynyl groups.	
1	I 17. The compound according to claim 15, wh	perein 7 is an _NP 14
2	A B • • • • • • • • • • • • • • • • • • •	erem 2 is an -ivit
	· Broat.	
1	18. The compound according to any of claims	40-43, wherein R ¹
2	2 is selected from the group consisting of -H, substituted and unsu	ıbstituted alkoxy
3	groups, substituted and unsubstituted heterocyclylalkoxy groups	, substituted and
4	unsubstituted heterocyclyloxy groups, and substituted and unsub	stituted heterocyclyl
5	groups.	
1	19. The compound according to claim 15, wh	erein R ² is selected

2 from the group consisting of H, F, Cl, -NO2, substituted and unsubstituted

heterocyclyl groups, and substituted and unsubstituted heterocyclylalkoxy groups.

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- 1 20. The compound according to claim 15, wherein R⁶ or R⁷ is an 2 alkyl group.
- 1 21. The compound according to claim 15, wherein R⁶ or R⁷ is an
- 2 -OR¹⁹ group and R¹⁹ is an alkyl group, an aryl group, a heterocyclyl group, or a
- 3 heterocyclylalkyl group.
- 1 22. A compound having the structure I, a tautomer of the
- 2 compound, a pharmaceutically acceptable salt of the compound, or a
- 3 pharmaceutically acceptable salt of the tautomer

$$\mathbb{R}^{2}$$
 \mathbb{R}^{3}
 \mathbb{R}^{4}
 \mathbb{R}^{9}
 \mathbb{R}^{5}
 \mathbb{R}^{6}
 \mathbb{R}^{7}

I

4

5

14

wherein,

6 Y is selected from the group consisting of -OH, SH, alkylthio groups, arylthio groups, $-OR^{10}$ groups, $-C(=O)-R^{11}$ groups, $-NR^{12}R^{13}$ 7 8 groups, -CN, substituted and unsubstituted alkyl groups, substituted 9 and unsubstituted alkenyl groups, substituted and unsubstituted 10 alkynyl groups, substituted and unsubstituted aralkyl groups, 11 substituted and unsubstituted heterocyclylalkyl groups, substituted 12 and unsubstituted alkylaminoalkyl groups, substituted and 13 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted

arylaminoalkyl groups, substituted and unsubstituted

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15	diarylaminoalkyl groups, substituted and unsubstituted
16	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
17	heterocyclylaminoalkyl groups, substituted and unsubstituted
18	heterocyclyl groups, substituted and unsubstituted aryl groups,
19	substituted and unsubstituted heterocyclyloxyalkyl groups, substituted
20	and unsubstituted hydroxyalkyl groups, substituted and unsubstituted
21	alkoxyalkyl groups, and substituted and unsubstituted aryloxyalkyl
22	groups;
23	Z is selected from the group consisting of O, S, and NR ¹⁴ groups;
24	R ¹ , R ² , R ³ , and R ⁴ may be the same or different and are
25	independently selected from the group consisting of H, Cl, Br, F, I,
26	-CN, -NO ₂ , -OH, -OR ¹⁵ groups, -NR ¹⁶ R ¹⁷ groups, substituted and
27	unsubstituted amidinyl groups, substituted and unsubstituted
28	guanidinyl groups, substituted and unsubstituted primary, secondary,
29	and tertiary alkyl groups, substituted and unsubstituted aryl groups,
30	substituted and unsubstituted alkenyl groups, substituted and
31	unsubstituted alkynyl groups, substituted and unsubstituted
32	heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,
33	substituted and unsubstituted alkylaminoalkyl groups, substituted and
34	unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted
35	arylaminoalkyl groups, substituted and unsubstituted
36	diarylaminoalkyl groups, substituted and unsubstituted
37	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
38	heterocyclylalkyl groups, and $-C(=O)R^{18}$ groups;
39	R ⁵ , R ⁶ , R ⁷ , and R ⁸ may be the same or different and are
40	independently selected from the group consisting of H, Cl, Br, F, I,
41	-NO ₂ , -OH, -OR ¹⁹ groups, -NR ²⁰ R ²¹ groups, -SH, -SR ²² groups,
42	$-S(=O)R^{23}$ groups, $-S(=O)_2R^{24}$ groups, -CN, substituted and

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43	unsubstituted amidinyl groups, substituted and unsubstituted
44	guanidinyl groups, substituted and unsubstituted primary, secondary
45	and tertiary alkyl groups, substituted and unsubstituted aryl groups,
46	substituted and unsubstituted alkenyl groups, substituted and
47	unsubstituted alkynyl groups, substituted and unsubstituted
48	heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl
49	groups, substituted and unsubstituted dialkylaminoalkyl groups,
50	substituted and unsubstituted arylaminoalkyl groups, substituted and
51	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted
52	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
53	heterocyclylalkyl groups, -C(=O)R ²⁵ groups, substituted and
54	unsubstituted aminoalkyl groups, substituted and unsubstituted
55	heterocyclylaminoalkyl groups, substituted and unsubstituted
56	hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl
57	groups, substituted and unsubstituted aryloxyalkyl groups, and
58	substituted and unsubstituted heterocyclyloxyalkyl groups;
59	R ⁹ and R ¹⁴ may be the same or different and are independently
60	selected from the group consisting of H, -OH, substituted and
61	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy
62	groups, -NH2, substituted and unsubstituted alkylamino groups,
63	substituted and unsubstituted arylamino groups, substituted and
64	unsubstituted dialkylamino groups, substituted and unsubstituted
65	diarylamino groups, substituted and unsubstituted (alkyl)(aryl)amino
66	groups, substituted and unsubstituted alkyl groups, substituted and
67	unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, and
68	-C(=O)-aryl groups;
69	R ¹⁰ is selected from the group consisting of substituted and
70	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,
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12	unsubstituted heterocyclylalkyl groups, $-C(=O)H$, $-C(=O)$ -alkyl		
73	groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl		
74	groups, -C(=0)NH ₂ , -C(=0)NH(alkyl) groups, -C(=0)NH(aryl)		
7 5	groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups,		
76	-C(=O)N(alkyl)(aryl) groups, -NH2, -NH(alkyl) groups, -NH(aryl)		
77	groups, -N(alkyl)2 groups, -N(alkyl)(aryl) groups, -N(aryl)2 groups,		
78	-C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl) ₂ groups,		
79	-C(=O)N(alkyl)(heterocyclyl) groups, and		
80	-C(=O)N(aryl)(heterocyclyl) groups;		
81	R ¹¹ is selected from the group consisting of H, -OH, alkoxy groups,		
82	aryloxy groups, -NH2, -NH(alkyl) groups, -NH(aryl) groups,		
83	-N(alkyl)2 groups, -N(aryl)2 groups, -N(alkyl)(aryl) groups,		
84	substituted and unsubstituted alkyl groups, -NH(heterocyclyl) groups,		
85	-N(heterocyclyl)2 groups, -N(alkyl)(heterocyclyl) groups, and		
86	substituted and unsubstituted aryl groups;		
87	R ¹² is selected from the group consisting of H, substituted and		
88	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,		
89	and substituted and unsubstituted heterocyclyl groups;		
90	R ¹³ is selected from the group consisting of H, substituted and		
91	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,		
92	substituted and unsubstituted heterocyclyl groups, -OH, alkoxy		
93	groups, aryloxy groups, -NH2, substituted and unsubstituted		
94	heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl		
95	groups, substituted and unsubstituted alkylaminoalkyl groups,		
96	substituted and unsubstituted dialkylaminoalkyl groups, substituted		
97	and unsubstituted arylaminoalkyl groups, substituted and		
98	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted		
99	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted		

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100	alkylamino groups, substituted and unsubstituted arylamino groups,		
101	substituted and unsubstituted dialkylamino groups, substituted and		
102	unsubstituted diarylamino groups, substituted and unsubstituted		
103	(alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups,		
104	-C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups,		
105	-C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,		
106	-C(=O)N(alkyl) ₂ groups, -C(=O)N(aryl) ₂ groups,		
107	-C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups,		
108	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,		
109	-C(=0)-N(heterocyclyl) ₂ groups, -C(=0)-N(alkyl)(heterocyclyl)		
110	groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and		
111	unsubstituted heterocyclylaminoalkyl groups, substituted and		
112	unsubstituted hydroxyalkyl groups, substituted and unsubstituted		
113	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl		
114	groups, and substituted and unsubstituted heterocyclyloxyalkyl		
115	groups;		
116	R ¹⁵ and R ¹⁹ may be the same or different and are independently		
117	selected from the group consisting of substituted and unsubstituted		
118	alkyl groups, substituted and unsubstituted aryl groups, substituted		
119	and unsubstituted heterocyclyl groups, substituted and unsubstituted		
120	heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups,		
121	-C(=O)-aryl groups, -C(=O)NH ₂ , -C(=O)NH(alkyl) groups,		
122	$-C(=O)NH(aryl)$ groups, $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$		
123	groups, -C(=O)N(alkyl)(aryl) groups, substituted and unsubstituted		
124	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl		
125	groups, substituted and unsubstituted dialkylaminoalkyl groups,		
126	substituted and unsubstituted arylaminoalkyl groups, substituted and		
127	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted		
128	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted		
129	heterocyclylaminoalkyl, substituted and unsubstituted		

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130	diheterocyclylaminoalkyl, substituted and unsubstituted	
131	(heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted	
132	(heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted	
133	alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl	
134	groups, substituted and unsubstituted aryloxyalkyl groups, and	
135	substituted and unsubstituted heterocyclyloxyalkyl groups;	
136	\mathbf{R}^{16} and \mathbf{R}^{20} may be the same or different and are independently	
137	selected from the group consisting of H, substituted and unsubstitute	
138	alkyl groups, substituted and unsubstituted aryl groups, and	
139	substituted and unsubstituted heterocyclyl groups;	
140	R ¹⁷ and R ²¹ may be the same or different and are independently	
141	selected from the group consisting of H, substituted and unsubstituted	
142	alkyl groups, substituted and unsubstituted aryl groups, substituted	
143	and unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl	
144	groups, $-C(=O)$ -aryl groups, $-C(=O)NH_2$, $-C(=O)NH$ (alkyl)	
145	groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl) ₂ groups,	
146	-C(=O)N(aryl)2 groups, -C(=O)N(alkyl)(aryl) groups,	
147	-C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and	
148	unsubstituted heterocyclylalkyl groups, substituted and unsubstituted	
149	aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl	
150	groups, substituted and unsubstituted dialkylaminoalkyl groups,	
151	substituted and unsubstituted arylaminoalkyl groups, substituted and	
152	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted	
153	(alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,	
154	-C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,	
155	-C(=O)-N(heterocyclyl) ₂ groups, -C(=O)-N(alkyl)(heterocyclyl)	
156	groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and	
157	unsubstituted heterocyclylaminoalkyl groups, substituted and	
158	unsubstituted hydroxyalkyl groups, substituted and unsubstituted	

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159	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl		
160	groups, and substituted and unsubstituted heterocyclyloxyalkyl		
161	groups;		
	_ 19 _ 02 _ 04		
162	R ¹⁸ , R ²³ , R ²⁴ , and R ²⁵ may be the same or different and are		
163	independently selected from the group consisting of H, -NH2,		
164	-NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)2 groups, -N(aryl)2		
165	groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,		
166	-N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,		
167	-N(heterocyclyl)2 groups, substituted and unsubstituted alkyl groups,		
168	substituted and unsubstituted aryl groups, -OH, substituted and		
169	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy		
170	groups, substituted and unsubstituted heterocyclyl groups, -NHOH,		
171	-N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups,		
172	-N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and -N(aryl)O-aryl		
173	groups; and		
174	R ²² is selected from the group consisting of substituted and		
175	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,		
176	and substituted and unsubstituted heterocyclyl groups,		
177	and further wherein, at least one of R ¹ , R ² , R ³ , or R ⁴ is an -OR ¹⁵		
178	group and R15 is selected from the group consisting of substituted and		
179	unsubstituted heterocyclylalkyl groups, substituted and unsubstituted		
180	dialkylaminoalkyl groups, substituted and unsubstituted		
181	alkylaminoalkyl groups, substituted and unsubstituted aminoalkyl		
182	groups, substituted and unsubstituted diarylaminoalkyl groups,		
183	substituted and unsubstituted arylaminoalkyl groups, substituted and		
184	unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and		
185	unsubstituted heterocyclyl groups, substituted and unsubstituted		
186	heterocyclylaminoalkyl groups, substituted and unsubstituted		

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187	diheterocyclylaminoalkyl groups, substituted and unsubstituted		
188	(heterocyclyl)(alkyl)aminoalkyl groups, and substituted and		
189	unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.		
1	23. The compound according to claim 22, wherein R ¹ is an -OR ¹⁵		
2	group and R ¹⁵ is selected from the group consisting of substituted and unsubstituted		
3	heterocyclylalkyl groups, substituted and unsubstituted dialkylaminoalkyl groups,		
4	substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted		
5	aminoalkyl groups, substituted and unsubstituted diarylaminoalkyl groups,		
6	substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted		
7	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted heterocyclyl groups,		
8	substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and		
9	unsubstituted diheterocyclylaminoalkyl groups, substituted and unsubstituted		
10	(heterocyclyl)(alkyl)aminoalkyl groups, and substituted and unsubstituted		
11	(heterocyclyl)(aryl)aminoalkyl groups.		
1	24. The compound according to claim 22, wherein Z is an -NR ¹⁰		
2	group.		
1	25. The compound according to claim 22, wherein R ¹ is selected		
2	from the group consisting of -H, substituted and unsubstituted alkoxy groups,		
3	substituted and unsubstituted heterocyclylalkoxy groups, substituted and		
4	unsubstituted heterocyclyloxy groups, and substituted and unsubstituted heterocyclyl		
5	groups.		
1	26. The compound according to claim 22, wherein R ² is selected		
2	from the group consisting of H, F, Cl, -NO ₂ , substituted and unsubstituted		
3	heterocyclyl groups, and substituted and unsubstituted heterocyclylalkoxy groups.		

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- 1 27. The compound according to claim 22, wherein R^6 or R^7 is an
- 2 alkyl group.
- 1 28. The compound according to claim 22, wherein R^6 or R^7 is an
- 2 -OR¹⁹ group and R¹⁹ is an alkyl group, an aryl group, a heterocyclyl group, or a
- 3 heterocyclylalkyl group.
- 1 29. A compound having the structure II, a tautomer of the
- 2 compound, a pharmaceutically acceptable salt of the compound, or a
- 3 pharmaceutically acceptable salt of the tautomer

$$R^{2}$$
 R^{3}
 R^{4}
 R^{9}
 R^{5}
 R^{6}
 R^{6}
 R^{6}
 R^{8}

4 II

5 wherein,

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6 Y is selected from the group consisting of H, -OH, -OR¹⁰ groups. -SH, -SR¹¹ groups, -NR¹²R¹³ groups, -CN, -C(=0)-R¹⁴ groups, 7 8 substituted and unsubstituted alkyl groups, substituted and 9 unsubstituted alkenyl groups, substituted and unsubstituted alkynyl 10 groups, substituted and unsubstituted aralkyl groups, substituted and 11 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted 12 alkylaminoalkyl groups, substituted and unsubstituted 13 dialkylaminoalkyl groups, substituted and unsubstituted

arylaminoalkyl groups, substituted and unsubstituted

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15	diarylaminoalkyl groups, substituted and unsubstituted		
16	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted		
17	heterocyclylaminoalkyl groups, substituted and unsubstituted		
18	heterocyclyl groups, substituted and unsubstituted aryl groups,		
19	substituted and unsubstituted hydroxyalkyl groups, substituted and		
20	unsubstituted alkoxyalkyl groups, substituted and unsubstituted		
21	aryloxyalkyl groups, and substituted and unsubstituted		
22	heterocyclyloxyalkyl groups;		
23	X^1 , X^2 , X^3 , and X^4 are selected from the group consisting of C and		
24	N, wherein at least one of X ¹ , X ² , X ³ , or X ⁴ is N;		
25	R ¹ , R ² , R ³ , R ⁴ , R ⁵ , R ⁶ , R ⁷ , and R ⁸ may be the same or different and		
26	are independently selected from the group consisting of H, Cl, Br, F		
27	I, -NO ₂ , -CN, -OH, -OR ¹⁵ groups, -NR ¹⁶ R ¹⁷ groups, -C(=O)R ¹⁸		
28	groups, -SH, -SR ¹⁹ groups, -S(=O)R ²⁰ groups, S(=O) ₂ R ²¹ groups,		
29	substituted and unsubstituted amidinyl groups, substituted and		
30	unsubstituted guanidinyl groups, substituted and unsubstituted		
31	primary, secondary, and tertiary alkyl groups, substituted and		
32	unsubstituted aryl groups, substituted and unsubstituted alkenyl		
33	groups, substituted and unsubstituted alkynyl groups, substituted and		
34	unsubstituted heterocyclyl groups, substituted and unsubstituted		
35	alkylaminoalkyl groups, substituted and unsubstituted		
36	dialkylaminoalkyl groups, substituted and unsubstituted		
37	arylaminoalkyl groups, substituted and unsubstituted		
38	diarylaminoalkyl groups, substituted and unsubstituted		
39	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted		
40	heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl		
41	groups, substituted and unsubstituted heterocyclylaminoalkyl groups,		
42	substituted and unsubstituted hydroxyalkyl groups, substituted and		
43	unsubstituted alkoxyalkyl groups, substituted and unsubstituted		

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44	aryloxyalkyl groups, and substituted and unsubstituted	
45	heterocyclyloxyalkyl groups; R ⁵ is absent or is H if X ¹ is N; R ⁶ is	
46	absent or is H if X ² is N; R ⁷ is absent or is H if X ³ is N; and R ⁸ is	
47	absent or is H if X ⁴ is N;	
48	R9 is selected from the group consisting of H, -OH, substituted and	
49	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy	
50	groups, -NH2, substituted and unsubstituted alkylamino groups,	
51	substituted and unsubstituted arylamino groups, substituted and	
52	unsubstituted dialkylamino groups, substituted and unsubstituted	
53	diarylamino groups, substituted and unsubstituted (alkyl)(aryl)amino	
54	groups, substituted and unsubstituted alkyl groups, substituted and	
55	unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, and	
56	-C(=O)-aryl groups;	
57	R ¹⁰ is selected from the group consisting of substituted and	
58	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,	
59	substituted and unsubstituted heterocyclyl groups, substituted and	
60	unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl	
61	groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl	
62	groups, -C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)	
63	groups, -C(=O)N(alkyl) ₂ groups, -C(=O)N(aryl) ₂ groups,	
64	-C(=O)N(alkyl)(aryl) groups, -NH2, -NH(alkyl) groups, -NH(aryl)	
65	groups, -N(alkyl)2 groups, -N(alkyl)(aryl) groups, -N(aryl)2 groups,	
66	-C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl) ₂ groups,	
67	-C(=O)N(alkyl)(heterocyclyl) groups, and	
68	-C(=O)N(aryl)(heterocyclyl) groups;	
69	R ¹¹ and R ¹⁹ may be the same or different and are independently	
70	selected from the group consisting of substituted and unsubstituted	
71	alkyl groups, and substituted and unsubstituted aryl groups;	

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R¹² is selected from the group consisting of H, substituted and 72 73 unsubstituted alkyl groups, substituted and unsubstituted aryl groups, 74 and substituted and unsubstituted heterocyclyl groups; R¹³ is selected from the group consisting of H, substituted and 75 76 unsubstituted alkyl groups, substituted and unsubstituted aryl groups. 77 substituted and unsubstituted heterocyclyl groups, -OH, alkoxy 78 groups, aryloxy groups, -NH2, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl 79 80 groups, substituted and unsubstituted alkylaminoalkyl groups, 81 substituted and unsubstituted dialkylaminoalkyl groups, substituted 82 and unsubstituted arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl groups, substituted and unsubstituted 83 84 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted 85 alkylamino groups, substituted and unsubstituted arylamino groups, 86 substituted and unsubstituted dialkylamino groups, substituted and 87 unsubstituted diarylamino groups, substituted and unsubstituted 88 (alkyl)(aryl)amino groups, -C(=0)H, -C(=0)-alkyl groups, 89 . -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, 90 $-C(=O)NH_2$, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups. 91 $-C(=O)N(alkyl)_2$ groups, $-C(=O)N(aryl)_2$ groups, 92 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, 93 -C(=0)-O-heterocyclyl groups, -C(=0)NH(heterocyclyl) groups. 94 $-C(=O)-N(heterocyclyl)_2$ groups, -C(=O)-N(alkyl)(heterocyclyl)95 groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and 96 unsubstituted heterocyclylaminoalkyl groups, substituted and 97 unsubstituted hydroxyalkyl groups, substituted and unsubstituted 98 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl 99 groups, and substituted and unsubstituted heterocyclyloxyalkyl 100 groups;

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101	R' is selected from the group consisting of H, -OH, alkoxy groups,		
102	aryloxy groups, -NH2, -NH(alkyl) groups, -NH(aryl) groups,		
103	-N(alkyl)2 groups, -N(aryl)2 groups, -N(alkyl)(aryl) groups,		
104	substituted and unsubstituted alkyl groups, substituted and		
105	unsubstituted aryl groups, -NH(heterocyclyl) groups,		
106	-N(heterocyclyl)2 groups, -N(alkyl)(heterocyclyl) groups, and		
107	-N(aryl)(heterocyclyl) groups;		
108	R ¹² and R ¹³ may join together to form a 5 to 7 membered saturated or		
109	unsaturated, substituted or unsubstituted N-containing ring;		
110	R ¹⁵ is selected from the group consisting of substituted and		
111	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,		
112	substituted and unsubstituted heterocyclyl groups, substituted and		
113	unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl		
114	groups, -C(=O)-aryl groups, -C(=O)NH ₂ , -C(=O)NH(alkyl)		
115	groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl) ₂ groups,		
116	-C(=O)N(aryl) ₂ groups, -C(=O)N(alkyl)(aryl) groups, substituted		
117	and unsubstituted aminoalkyl groups, substituted and unsubstituted		
118	alkylaminoalkyl groups, substituted and unsubstituted		
119	dialkylaminoalkyl groups, substituted and unsubstituted		
120	arylaminoalkyl groups, substituted and unsubstituted		
121	diarylaminoalkyl groups, substituted and unsubstituted		
122	(alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted		
123	heterocyclylaminoalkyl groups, substituted and unsubstituted		
124	diheterocyclylaminoalkyl groups, substituted and unsubstituted		
125	(heterocyclyl)(alkyl)aminoalkyl groups, substituted and unsubstituted		
126	(heterocyclyl)(aryl)aminoalkyl groups, substituted and unsubstituted		
127	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl		
128	groups, substituted and unsubstituted hydroxyalkyl groups, and		
129	substituted and unsubstituted heterocyclyloxyalkyl groups;		

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130	R ¹⁶ is selected from the group consisting of H, substituted and		
131	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,		
132	and substituted and unsubstituted heterocyclyl groups;		
133	R ¹⁷ is selected from the group consisting of H, substituted and		
134	unsubstituted alkyl groups, substituted and unsubstituted aryl groups,		
135	substituted and unsubstituted heterocyclyl groups, OH, substituted		
136	and unsubstituted alkoxy groups, substituted and unsubstituted		
137	aryloxy groups, -NH ₂ , -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl		
138	groups, -C(=O)NH ₂ , -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)		
139	groups, -C(=O)N(alkyl)2 groups, -C(=O)N(aryl)2 groups,		
140	-C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups,		
141	-C(=O)O-aryl groups, substituted and unsubstituted aminoalkyl		
142	groups, substituted and unsubstituted alkylaminoalkyl groups,		
143	substituted and unsubstituted dialkylaminoalkyl groups, substituted		
144	and unsubstituted arylaminoalkyl groups, substituted and		
145	unsubstituted diarylaminoalkyl groups, substituted and unsubstituted		
146	(aryl)(alkyl)aminoalkyl groups, substituted and unsubstituted		
147 ·	heterocyclylalkyl groups, -C(=O)-heterocyclyl groups,		
148	-C(=O)-Oheterocyclyl groups, -C(=O)NH(heterocyclyl) groups,		
149	-C(=O)-N(heterocyclyl)2 groups, -C(=O)-N(alkyl)(heterocyclyl)		
150	groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and		
151	unsubstituted heterocyclylaminoalkyl groups, substituted and		
152	unsubstituted hydroxyalkyl groups, substituted and unsubstituted		
153	alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl		
154	groups, and substituted and unsubstituted heterocyclyloxyalkyl		
155	groups;		
156 ·	R ¹⁶ and R ¹⁷ may join together to form a 5 to 7 membered saturated or		
157	unsaturated, substituted or unsubstituted N-containing ring; and		

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158	R ¹⁸ , R ²⁰ , and R ²¹ may be the same or different and are independently		
159	selected from the group consisting of H, -NH2, -NH(alkyl) groups,		
160	-NH(aryl) groups, -N(alkyl)2 groups, -N(aryl)2 groups,		
161	-N(alkyl)(aryl) groups, substituted and unsubstituted alkyl groups,		
162	substituted and unsubstituted aryl groups, -OH, substituted and		
163	unsubstituted alkoxy groups, substituted and unsubstituted aryloxy		
164	groups, substituted and unsubstituted heterocyclyl groups, -NHOH,		
165	-N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups,		
166	-N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and -N(aryl)O-aryl		
167	groups.		
-1	30. The compound according to claim 29, wherein Y is selected		
2	from the group consisting of H, -OH, -OR 10 groups, and -NR 12R 13 groups.		
•			
1	31. The compound according to claim 29, at least two of X^1 , X^2 , X^3 and X^4 are C and the compound according to claim 29, at least two of X^1 , X^2 ,		
2	X ³ , and X ⁴ are C and the corresponding substituents R ⁵ , R ⁶ , R ⁷ , and R ⁸ are		
5	hydrogen, and at least one of X^1 , X^2 , X^3 , and X^4 is N.		
1	32. The compound according to claim 29, wherein R ⁶ or R ⁷ is an		
2	alkyl group.		
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1	33. The compound according to claim 29, wherein R ⁶ or R ⁷ is an		
2	-OR ¹⁵ group and R ¹⁵ is an alkyl, aryl, heterocyclyl, or heterocyclylalkyl group.		
1	34. The compound according to claim 29, wherein R ¹ is selected		
2	from the group consisting of H, substituted and unsubstituted alkoxy groups,		
3	substituted and unsubstituted heterocyclylalkoxy groups, substituted and		
4	unsubstituted heterocyclyloxy groups, and substituted and unsubstituted heterocyclyl		
5	groups.		

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l	35. The compound according to claim 29, wherein R ² is selected		
2	from the group consisting of H, F, Cl, -NO2, substituted and unsubstituted		
3	heterocyclyl groups, and substituted and unsubstituted heterocyclylalkoxy groups		
l	36. A pharmaceutical formulation, comprising the compound		
2	according to any of claims 1, 8, 15, 22, or 29 in combination with a		
3	pharmaceutically acceptable carrier.		
L	37. A method of treating a patient in need of an inhibitor of		
2	vascular endothelial growth factor receptor tyrosine kinase, comprising		
3	administering an effective amount of the pharmaceutical formulation according to		
ļ	claim 36 to a patient in need thereof.		

INTERNATIONAL SEARCH REPORT

inf ional Application No PCT/US 01/42131

A. CLASSII IPC 7	FICATION OF SUBJECT MATTER C07D401/04 C07D409/	04 A61K31/4704		
According to	h (nternational Patent Classification (IPC) or to both national classification	tion and IPC		
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Minimum do IPC 7	cumentation searched (classification system followed by classification ${\tt CO7D}$	n symbols)	·	
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C. DOCUME	ENTS CONSIDERED TO BE RELEVANT			
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Special ca	ntegories of chied documents:	"T" later document published after the inte		
	ent defining the general state of the art which is not dered to be of particular relevance	or priority date and not in conflict with cited to understand the principle or the invention		
	document but published on or after the international	"X" document of particular relevance; the cannot be considered novel or cannot	taimed invention the considered to	
"L" docume which citation	"L" document which may throw doubts on priority claim(s) or involve an inventive step when the document is taken alone which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention claim or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the			
*Or document referring to an oral disclosure, use, exhibition or document is combined with one or more other such documents, such combination being obvious to a person skilled				
P document published prior to the International filing date but in the erf. **Street than the priority date claimed **Street than the priority date claimed **Street than the priority date claimed **Street than the priority date claimed **Street than the erf.				
Date of the	actual completion of the international search	Date of mailing of the international sea	arch report	
2	27 February 2002 06/03/2002			
Name and mailing address of the ISA Authorized officer				
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx 31 651 epo nl, Fax: (+31-70) 340-3016 Kyriakakou, G				

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